	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definitio	Errors
1	BRS	L1	341	apolipoprotein adj a-i	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 18:11			0
2	BRS	L2	1	linker same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 18:12			0
3	BRS	L3	7	1 same (fusion adj protein)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 18:21			0
4	BRS	L4	60	antibody same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 18:21			0
5	BRS	L5	7	antibody same 1 same fusion	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 18:24			0
6	BRS	L6	0	1 same conjugate	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 18:24			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definitio	Errors
1	BRS	L4	1	wo-200181376-$.did.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 17:28			0
2	BRS	L5	341	apolipoprotein adj a-i	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 17:26			0
3	BRS	L6	51490	fc	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 17:26			0
4	BRS	L7	1386	fc adj domain	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 17:27			0
5	BRS	L8	220826	(polyethylene adj glycol) or peg or polylysine or dextran	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 17:28			0
6	BRS	L10	1	9 same (conjugate or link$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 17:29			0
7	BRS	L9	8	5 same (7 or 8)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/08 17:29			0

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FILE 'MEDLINE' ENTERED AT 19:05:1[redacted]N 08 JUL 2003

FILE 'CAPLUS' ENTERED AT 19:05:16 ON 08 JUL 2003
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FILE 'AGRICOLA' ENTERED AT 19:05:16 ON 08 JUL 2003

=> s apo-ai amphipathic helix peptide
L1            1 APO-AI AMPHIPATHIC HELIX PEPTIDE

=> d l1 1 ibib abs

L1   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2001:798252  CAPLUS
DOCUMENT NUMBER:          135:362518
TITLE:                    Apo-AI/AII peptide derivatives for hypocholesteremic
                          and antiviral therapy
INVENTOR(S):              Kohno, Tadahiko
PATENT ASSIGNEE(S):       Amgen Inc., USA
SOURCE:                   PCT Int. Appl., 49 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

      PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
      ---------------   ----  --------      ---------------  --------
      WO 2001081376      A2   20011101      WO 2001-US13068  20010423
      WO 2001081376      A3   20030109
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
              HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
              LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
              RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
              YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
              BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
      US 2003040470      A1   20030227      US 2001-840669   20010423
      EP 1290013         A2   20030312      EP 2001-930664   20010423
          R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.:                    US 2000-198920P  P  20000421
                                          WO 2001-US13068  W  20010423
AB    The present invention concerns therapeutic agents that mimic the activity
      of   ***Apo***  -  ***AI***     ***amphipathic***     ***helix***
        ***peptide***  .  In accordance with the present invention, the compds. of
      the invention comprise: (a) a   ***Apo***  -  ***AI***
        ***amphipathic***     ***helix***     ***peptide***   or   ***Apo***  -
        ***AI***     ***amphipathic***     ***helix***     ***peptide***  -mimetic
      domain, preferably the amino acid sequence of SEQ ID NO:7, or sequences
      derived therefrom by phage display, RNA-peptide screening, or the other
      techniques mentioned above; and (b) a vehicle, such as a polymer (e.g.,
      PEG or dextran) or an Fc domain, which is preferred; wherein the vehicle,
      preferably an Fc domain, is covalently attached to the   ***Apo***  -
        ***AI***     ***amphipathic***     ***helix***     ***peptide***   or
        ***Apo***  -  ***AI***     ***amphipathic***     ***helix***
        ***peptide***  -mimetic domain.  The vehicle and the   ***Apo***  -
        ***AI***     ***amphipathic***     ***helix***     ***peptide***   or
        ***Apo***  -  ***AI***     ***amphipathic***     ***helix***
        ***peptide***  -mimetic domain may be linked through the N- or C-terminus
      of the   ***Apo***  -  ***AI***     ***amphipathic***     ***helix***
        ***peptide***   or   ***Apo***  -  ***AI***     ***amphipathic***
        ***helix***     ***peptide***  -mimetic domain, as described further
```

below. The preferred vehicle is an Fc domain, and the preferred Fc domain is an IgG Fc domain. Prefer ***Apo*** - ***AI*** ***amphipathic*** ***helix*** ***peptide*** or ***Apo*** - ***AI*** ***amphipathic*** ***helix*** ***peptide*** -mimetic domains comprise the amino acid sequences described in Table 1. Other ***Apo*** - ***AI*** ***amphipathic*** ***helix*** ***peptide*** or ***Apo*** - ***AI*** ***amphipathic*** ***helix*** ***peptide*** -mimetic domains can be generated by phage display, RNA-peptide screening and the other techniques mentioned herein.

=> d his

(FILE 'HOME' ENTERED AT 19:04:55 ON 08 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 19:05:16 ON 08 JUL 2003
L1 1 S APO-AI AMPHIPATHIC HELIX PEPTIDE

=> s apo-ai
L2 2542 APO-AI

=> s l2 (p) amphipathic (p) peptide
L3 19 L2 (P) AMPHIPATHIC (P) PEPTIDE

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 8 DUPLICATE REMOVE L3 (11 DUPLICATES REMOVED)

=> d l4 1-8 ibib abs

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:798252 CAPLUS
DOCUMENT NUMBER: 135:362518
TITLE: Apo-AI/AII peptide derivatives for hypocholesteremic and antiviral therapy
INVENTOR(S): Kohno, Tadahiko
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081376	A2	20011101	WO 2001-US13068	20010423
WO 2001081376	A3	20030109		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003040470	A1	20030227	US 2001-840669	20010423
EP 1290013	A2	20030312	EP 2001-930664	20010423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-198920P P 20000421
WO 2001-US13068 W 20010423

AB The present invention concerns therapeutic agents that mimic the activity of ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide***. In accordance with the present invention, the compds. of the invention comprise: (a) a ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** or ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** -mimetic domain, preferably the amino acid sequence of SEQ ID NO:7, or sequences derived therefrom by phage display, RNA-***peptide*** screening, or the other techniques mentioned above; and (b) a vehicle, such as a polymer (e.g., PEG or dextran) or an Fc domain, which is preferred; wherein the vehicle, preferably an Fc domain, is covalently attached to the ***Apo*** - ***AI*** ***amphipathic***

helix ***peptide*** or ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** -mimetic domain. The vehicle and the ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** or ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** -mimetic domain may be linked through the N- or C-terminus of the ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** or ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** -mimetic domain, as described further below. The preferred vehicle is an Fc domain, and the preferred Fc domain is an IgG Fc domain. Preferred ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** or ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** -mimetic domains comprise the amino acid sequences described in Table 1. Other ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** or ***Apo*** - ***AI*** ***amphipathic*** helix ***peptide*** -mimetic domains can be generated by phage display, RNA- ***peptide*** screening and the other techniques mentioned herein.

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:539120 CAPLUS
DOCUMENT NUMBER: 129:300381
TITLE: Contribution of apo AII and LCAT oblique peptides to HDL metabolism
AUTHOR(S): Vanloo, B.; Perez-Mendez, O.; Lambert, G.; Tavernier, J.; Vandekerckhove, J.; Brasseur, R.; Rosseneu, M.
CORPORATE SOURCE: Department of Biochemistry, University of Gent, Ghent, Belg.
SOURCE: International Congress Series (1998), 1155(Atherosclerosis XI), 1155-1160
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Computer modeling of the apo ACC 53-70 and the LCAT 56-68 segments suggests that these ***amphipathic*** helixes are oriented at an angle of 30.degree. at a lipid/water interface, due to the N-C hydrophobicity gradient along the helix. Mutant ***peptides*** were designed by computer modeling to be parallel (0.degree.) or to retain the same orientation compared to a lipid bilayer. The capacity of the WT and variant ***peptides*** to induce fusion of pyrene-labeled PC/PE/chol vesicles was investigated. The excimer/monomer fluorescence ratio decreased under the addn. of all oblique-oriented ***peptides*** , while the 0.degree. ***peptide*** had no fusogenic activity. Release of calcein, entrapped inside the PC/PE/chol vesicles, was further demonstrated upon addn. of the apo ACC and LCAT oblique ***peptides*** . The apo ACC 53-70 ***peptide*** and the oblique variant displaced up to 55% ***apo*** ***AI*** from HDL3 as shown by gel filtration, whereas the 0.degree. variant had no effect, thus suggesting that the C-terminal apo ACC ***peptide*** is fusogenic and that it can displace ***apo*** ***AI*** from HDL3. The insertion of the C-terminal hydrophobic end of the LCAT ***peptide*** into the lipid phase was demonstrated by moving the W61 residue of LCAT to position 57 and 68, resp., and comparing the fluorescence properties of the variant ***peptides*** . The contribution of the 56-68 ***peptide*** to the enzymic activity of LCAT was investigated by constructing and expressing LCAT deletion and substitution mutants. Results obtained both with the synthetic ***peptide*** and with the LCAT mutants suggest that in native LCAT, this domain might contribute to the interfacial substrate recognition of the enzyme. It might help further in destabilizing the lipoprotein lipid core and enhancing the diffusion of a phospholipid monomer into the active site of the enzyme.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999076987 MEDLINE
DOCUMENT NUMBER: 99076987 PubMed ID: 9862171
TITLE: Branched synthetic peptide constructs mimic cellular binding and efflux of apolipoprotein AI in reconstituted high density lipoproteins.
AUTHOR: Nion S; Demoor L; Boutillon C; Luchoomun J; Vanloo B; Fievet C; Castro G; Rosseneu M; Fruchart J C; Tartar A; Clavey V
CORPORATE SOURCE: INSERM U325, Institut Pasteur de Lille et Faculte de Pharmacie, France.
SOURCE: ATHEROSCLEROSIS, (1998 Dec) 141 (2) 227-35.
Journal code: 0242543. ISSN: 0021-9150.
PUB. COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990225

AB This study investigates the suitability of the trimeric apolipoprotein (***apo***) ***AI*** (145-183) ***peptide*** that we recently described, to serve as a model to probe the relationship between apoAI structure and function. Three copies of the apoAI(145-183) unit, composed each of two ***amphipathic*** alpha-helical segments, were branched onto a covalent core matrix and the construct was recombined with phospholipids. A similar construct was made with the apoAI(102-140) ***peptide*** and used as a comparison with dimyristoylglycerophosphocholine (DMPC)-apoAI complexes. The DMPC-trimeric-apoAI(145-183) complexes had similar immunological reactivity with monoclonal antibodies directed against the 149-186 apoAI sequence (A44), suggesting that the A44 epitope is exposed similarly in both the synthetic ***peptide*** and the native apoAI complexes. The complexes generated with the trimeric-apoAI(145-183) bind specifically to HeLa cells with comparable affinity to the DMPC apoAI complexes; they are a good competitor for binding of apoAI to both HeLa cells and Fu5AH rat hepatoma cells; finally, these complexes promote cholesterol efflux from Fu5AH cells with an efficiency comparable with the ***apo*** ***AI*** /lipid complexes. To study LCAT activation by the trimeric ***apo*** ***AI*** (145-183) construct, complexes were prepared with dipalmitoylphosphatidylcholine (DPPC), cholesterol (C) and either the trimeric construct or apoAI. LCAT activation by the trimeric construct was much lower than by ***apo*** ***AI*** , possibly because the conformation of the trimeric 145-183 ***peptide*** in DPPC/C/ ***peptide*** complexes does not mimic that of apoAI in the corresponding complexes. In comparison, the complexes generated with the multimeric apoAI(102-140) construct had a poor capacity to mimic the physico-chemical and biological properties of apoAI. The apoAI(102-140) construct had low affinity for lipid compared with the (145-183) construct. After association with lipids, it was a poor competitor of DMPC-apoAI complexes for cellular binding and had only limited capacity to promote cholesterol efflux. These results suggest trimeric constructs can serve as an appropriate models for apoAI, enabling further investigations and new experimental approaches to determine the structure-function relationship of apoAI.

L4 ANSWER 4 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 96:404943 SCISEARCH
THE GENUINE ARTICLE: UL589
TITLE: BRAIN EXPRESSION OF APOLIPOPROTEIN-E, APOLIPOPROTEIN-J, AND APOLIPOPROTEIN-A-I IN ALZHEIMERS-DISEASE
AUTHOR: HARR S D; UINT L; HOLLISTER R; HYMAN B T (Reprint); MENDEZ A J
CORPORATE SOURCE: MASSACHUSETTS GEN HOSP, NEUROL SERV, WRN 408, BOSTON, MA, 02114 (Reprint); MASSACHUSETTS GEN HOSP, NEUROL SERV, BOSTON, MA, 02114; MASSACHUSETTS GEN HOSP, CARDIAC UNIT, BOSTON, MA, 02114
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NEUROCHEMISTRY, (JUN 1996) Vol. 66, No. 6, pp. 2429-2435.
ISSN: 0022-3042.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Inheritance of the epsilon 4 allele of apolipoprotein (apo) E is associated with increased risk of Alzheimer's disease (AD) and with increased beta-amyloid ***peptide*** (A beta) deposition in the cortex. Apo E is a member of a family of exchangeable apos, characterized by the presence of ***amphipathic*** alpha-helical segments that allow these molecules to act as surfactants on the surface of lipoprotein particles. Two members of this family, apo E and apo J, have been shown to bind soluble A beta, and both are associated with senile plaques in the AD cortex. We now have studied the pattern of brain apo expression and found that five members of this class are present: ***apo*** ***AI*** , A-IV, D, E, and J, By contrast, apos A-II, B, and C-II were not detectable. Immunohistochemistry revealed that, in addition to apo E and apo J, apo A-I immunostained occasional senile plaques in AD cortex. Immunoblot analysis showed no difference in the relative amounts of any of

these apos in tissue homogenates of frontal lobe from AD or control patients. Comparison by APO E genotype showed no differences in the amount of apo E in brain among APO E epsilon 3/3, epsilon 3/4, or epsilon 4/4 individuals; however, a significant decrease in the amount of apo J was associated with the APO E epsilon 4 allele. No differences in apo J levels were detected in CSF samples of AD subjects, We propose that several members of the exchangeable apo family may interact with A beta deposits in senile plaques through common ***amphipathic*** alpha-helical domains. Competition among these molecules for binding of A beta or A beta aggregates may influence the deposition of A beta in senile plaques.

L4 ANSWER 5 OF 8 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 95315183 MEDLINE
DOCUMENT NUMBER: 95315183 PubMed ID: 7794908
TITLE: Efflux of cellular cholesterol and phospholipid to lipid-free apolipoproteins and class A amphipathic peptides.
AUTHOR: Yancey P G; Bielicki J K; Johnson W J; Lund-Katz S; Palgunachari M N; Anantharamaiah G M; Segrest J P; Phillips M C; Rothblat G H
CORPORATE SOURCE: Department of Biochemistry, Medical College of Pennsylvania, Philadelphia 19129, USA.
CONTRACT NUMBER: HL07443 (NHLBI)
HL22633 (NHLBI)
HL34343 (NHLBI)
+
SOURCE: BIOCHEMISTRY, (1995 Jun 20) 34 (24) 7955-65.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950817
Last Updated on STN: 19980206
Entered Medline: 19950803

AB The mechanism(s) by which lipid-free apolipoprotein (***apo*** ***AI*** is able to stimulate efflux of cholesterol and phospholipid from cells in cultures has (have) been examined. This process was found to be enhanced when macrophages were enriched with cholesterol. There were 12- and 4-fold increases in cholesterol and phospholipid efflux, respectively, from cholesterol-enriched mouse macrophages when compared to cells not loaded with cholesterol. This enhancement in cholesterol efflux to lipid-free ***apo*** ***AI*** from macrophages enriched with cholesterol was found to be controlled by the level of free cholesterol in the cells. When cholesterol-enriched mouse macrophages were exposed to lipid-free ***apo*** ***AI*** at 20 micrograms/mL (706 nM), there was significant efflux of [14C]cholesterol and [3H]phospholipid (20% +/- 0.5%/24 h and 6% +/- 0.3%/24 h, respectively). In comparison, HDL at equivalent protein concentrations only stimulated 11% and 4% efflux of cholesterol and phospholipid, respectively. Synthetic ***peptides*** containing ***amphipathic*** helical segments that mimic those present in ***apo*** ***AI*** were used to examine the structural features of the apoprotein which stimulate lipid efflux. ***Peptides*** containing only one (18A) or two (37pA) ***amphipathic*** helical segments stimulated as much cholesterol efflux from both mouse macrophages and L-cells as ***apo*** ***AI*** . The order of efficiency, as assessed by the mass concentration at which half-maximal efflux was reached (EC50), was ***apo*** ***AI*** > 37pA > 18A, indicating that acceptor efficiency was dependent on the number of ***amphipathic*** helical segments per molecule. When the helical content of 18A was increased by neutralizing the charges at the ends of the ***peptide*** (Ac-18A-NH2), there was a substantial increase in the efficiency for cholesterol efflux (EC50 18A = 17 micrograms/mL vs Ac-18A-NH2 = 6 micrograms/mL). In contrast, when the amphipathicity of the helix in 18A was decreased by scrambling the amino acid sequence, thereby reducing its lipid affinity, cholesterol and phospholipid efflux were not stimulated. The efficiency with which the ***peptides*** stimulated cholesterol efflux was in order of their lipid affinity (37pA > Ac-18A-NH2 > 18A), and this order was similar for phospholipid efflux. The time course of lipid release from mouse macrophages and L-cells indicated that phospholipid appeared in the extracellular medium before cholesterol. These results suggest that the ***apo*** ***AI*** or ***peptides*** first interacted with the cell to form protein/phospholipid complexes, that could then accept cholesterol.

L4 ANSWER 6 OF 8 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 94364988 MEDLINE
DOCUMENT NUMBER: 94364988 PubMed ID: 8083197
TITLE: The influence of apolipoprotein structure on the efflux of cellular free cholesterol to high density lipoprotein.
AUTHOR: Davidson W S; Lund-Katz S; Johnson W J; Anantharamaiah G M; Palgunachari M N; Segrest J P; Rothblat G H; Phillips M C
CORPORATE SOURCE: Medical College of Pennsylvania, Department of Biochemistry, Philadelphia 19129.
CONTRACT NUMBER: HL07443 (NHLBI)
HL22633 (NHLBI)
HL34343 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Sep 16) 269 (37) 22975-82.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941021
Last Updated on STN: 19980206
Entered Medline: 19941011

AB The influence of apolipoprotein conformation on the ability of high density lipoprotein (HDL) to remove cellular free cholesterol (FC) has not been studied in detail. To address the effects of ***amphipathic*** alpha-helix structure on cellular FC efflux, three class A helical ***peptides*** and apolipoprotein (***apo***) ***AI*** were complexed to dimyristoyl phosphatidylcholine (DMPC) to make discoidal complexes that were used as acceptors of cell cholesterol. The ***peptides*** consisted of an 18-amino acid, ***amphipathic*** , alpha-helical ***peptide*** with the sequence DWLKAFYDKVAEKLKEAF (18A), a dimer of 18A covalently linked by a proline residue (37pA), and acetyl-18A-amide (Ac-18A-NH2) that has a higher alpha-helix content than the unblocked 18A molecule. The three ***peptides*** strongly mimic the lipid-binding characteristics of the ***amphipathic*** segments of apolipoproteins and form discoidal complexes with DMPC that are similar in diameter (11-12 nm) to those formed by human apoAI when reconstituted at a 2.5:1 (w:w) phospholipid to protein ratio. The abilities of these complexes to remove radiolabeled FC were compared in experiments using cultured mouse L-cell fibroblasts; efflux of FC from both the plasma membrane and the lysosomal pools was examined. For each of the acceptors, the removal of cholesterol from the plasma membrane and lysosomal pools was equally efficient. All four discoidal complexes were equally efficient cell membrane FC acceptors when compared at saturating acceptor concentrations of > 200 micrograms of DMPC/ml of medium. However, at the same lipid concentration, protein-free DMPC small unilamellar vesicles (SUV) were significantly less efficient. The initial rates of FC removal from cells at saturating concentrations of acceptor particles (Vmax) were 12, 10, 10, and 11% per h, respectively, for the complexes containing either 18A, Ac-18A-NH2, 37pA, or apoAI, but only 1% cellular FC per h for the DMPC SUV. The 10-fold higher Vmax for the apoprotein/ ***peptide*** -containing acceptors was likely due to a reversible interaction of apoprotein or ***peptide*** with the plasma membrane that changed the lipid packing characteristics in such a way as to increase the rate of FC desorption from the cell surface. This interaction required ***amphipathic*** alpha-helical segments, but it was not affected by the length, number, or lipid-binding affinity of the helices. Furthermore, the efflux efficiency was not dependent on the amino acid sequence of the helical segments which suggests that this interaction is not mediated by a specific cell surface binding site.(ABSTRACT TRUNCATED AT 400 WORDS)

L4 ANSWER 7 OF 8 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 91273815 MEDLINE
DOCUMENT NUMBER: 91273815 PubMed ID: 1905134
TITLE: An approach to the functional analysis of lecithin-cholesterol acyltransferase. Activation by recombinant normal and mutagenized apolipoprotein AI.
AUTHOR: Bruhn H; Stoffel W
CORPORATE SOURCE: Institut fur Biochemie, Medizinische Fakultat, Universitat zu Koln.
SOURCE: BIOLOGICAL CHEMISTRY HOPPE-SEYLER, (1991 Mar) 372 (3) 225-34.
Journal code: 8503054. ISSN: 0177-3593.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199108
ENTRY DATE: Entered STN: [redacted]0818
Last Updated on STN: 19980206
Entered Medline: 19910801

AB Apolipoprotein AI (***apo*** ***AI***) of human serum high-density lipoprotein functions as an activator of lecithin-cholesterol acyltransferase (LCAT) and therefore plays an important role in reversed cholesterol transport. The mechanism of the acyltransfer, the activating polypeptide domains of ***apo*** ***AI*** and the active site of LCAT in this transesterification are not yet known. Synthetic ***peptides*** of the ***apo*** ***AI*** sequence have been designed to determine the activating structure, but did not yet lead to conclusive results. This also applies to spontaneous ***apo*** ***AI*** mutants. We therefore used the method of site-directed mutagenesis of ***apo*** ***AI*** cDNAs using the overlap extension approach by the polymerase chain reaction. These constructs were cloned into the procaryotic vector pET8c and expressed under the inducible T7 promoter. The engineered ***apo*** ***AI*** polypeptides were isolated and purified by affinity chromatography and assayed for their activator activity. The essentials of this approach to the structure and function of activators in general have successfully been exemplified for the LCAT activation by engineering ***apo*** ***AI*** mutant polypeptides a) by the deletion of two adjacent ***amphipathic*** helices (amino acid residues 146-186) and b) by introducing a point mutation (Glu111----Gln).

L4 ANSWER 8 OF 8 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 86016095 MEDLINE
DOCUMENT NUMBER: 86016095 PubMed ID: 2995928
TITLE: The human apolipoprotein AII gene: structural organization and sites of expression.
AUTHOR: Knott T J; Wallis S C; Robertson M E; Priestley L M; Urdea M; Rall L B; Scott J
SOURCE: NUCLEIC ACIDS RESEARCH, (1985 Sep 11) 13 (17) 6387-98. Journal code: 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X02905
ENTRY MONTH: 198511
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19851104

AB The complete nucleotide sequence of the human apolipoprotein All gene together with 911 bases of 5' flanking sequence and 687 bases of 3' flanking sequence have been determined. The mRNA coding region is interrupted by three introns of 169, 293 and 395bp. The Intro-exon structure of the apo All gene is similar to that of the ***apo*** ***AI*** , apo CIII and apo E genes: three introns separate 4 coding sequences specifying the 5' untranslated region, pre- ***peptide*** , a short N-terminal domain and a C-terminal domain composed of a variable number of lipid-binding ***amphipathic*** helices. Intron II carries a 33bp dG-dT repetitive element adjacent to the 3' splice junction which has the potential to adopt the Z-DNA conformation. The 5' and 3' terminuses of the mRNA have been identified by primer extension and S1 nuclease mapping. A number of short direct repeats are found in the 5' flanking region and an inverted repeat occurs between the CAAT and TATA boxes. Downstream of the the gene is an Alu family repeat containing a polymorphic MspI site, the deletion of which is associated with increased circulating levels of apoAII. ApoAII gene expression was demonstrated in adult human liver and HepG2 cells but not in human small intestine. Of ten Rhesus monkey tissues examined apo All mRNA was detected only in liver.

=> d his

(FILE 'HOME' ENTERED AT 19:04:55 ON 08 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 19:05:16 ON 08 JUL 2003
L1 1 S APO-AI AMPHIPATHIC HELIX PEPTIDE
L2 2542 S APO-AI
L3 19 S L2 (P) AMPHIPATHIC (P) PEPTIDE
L4 8 DUPLICATE REMOVE L3 (11 DUPLICATES REMOVED)

L6 . . . 7 DUPLICATE REMOVE L5 (14 DUPLICATES REMOVED)
L7 1 S L6 NOT L4

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	37.09	37.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.95	-1.95

STN INTERNATIONAL LOGOFF AT 19:09:07 ON 08 JUL 2003

```
=> s l2 (p) helix (p) peptide
L5            21 L2 (P) HELIX (P) PEPTIDE

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L5
L6             7 DUPLICATE REMOVE L5 (14 DUPLICATES REMOVED)

=> s l6 not l4
L7             1 L6 NOT L4

=> d l7 1 ibib abs

L7   ANSWER 1 OF 1     MEDLINE
ACCESSION NUMBER:    1998237604     MEDLINE
DOCUMENT NUMBER:     98237604   PubMed ID: 9578492
TITLE:               The C-terminal helix of human apolipoprotein AII promotes
                     the fusion of unilamellar liposomes and displaces
                     apolipoprotein AI from high-density lipoproteins.
AUTHOR:              Lambert G; Decout A; Vanloo B; Rouy D; Duverger N;
                     Kalopissis A; Vandekerckhove J; Chambaz J; Brasseur R;
                     Rosseneu M
CORPORATE SOURCE:    CJF INSERM 9508, Universite Paris VI, France.
SOURCE:              EUROPEAN JOURNAL OF BIOCHEMISTRY, (1998 Apr 1) 253 (1)
                     328-38.
                     Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY:        GERMANY: Germany, Federal Republic of
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199805
ENTRY DATE:          Entered STN: 19980529
                     Last Updated on STN: 19980529
                     Entered Medline: 19980518
AB   To assess the functional properties of apolipoprotein (apo) AII and to
     investigate the mechanism leading to the displacement of   ***apo***
       ***AI***   from native and reconstituted high-density lipoproteins (HDL
     and r-HDL) by apo AII, wild-type and variant apo AII   ***peptides***
     were synthesized.  The wild-type   ***peptides***   , residues 53-70 and
     58-70, correspond to the C-terminal   ***helix***   of apo AII and are
     predicted to insert at a tilted angle into a lipid bilayer.  We
     demonstrate that both the apo AII-(53-70)   ***peptide***   , and to a
     lesser extent the apo AII-(58-70)   ***peptide***   are able to induce
     fusion of unilamellar lipid vesicles together with membrane leakage, and
     to displace   ***apo***     ***AI***   from HDL and r-HDL.  Two variants
     of the apo AII-(53-70)-wild-type (WT)   ***peptide***   , designed either
     to be parallel to the water/lipid interface [apo AII-(53-70)-0 degrees] or
     to retain an oblique orientation [apo AII-(53-70)-30 degrees], were
     synthesized in order to test the influence of the obliquity on their
     fusogenic properties and ability to displace   ***apo***     ***AI***
     from HDL.  The parallel variant did not bind lipids, due to its
     self-association properties.  However, the apo AII-(53-70)-30 degrees
     variant was fusogenic and promoted the displacement of   ***apo***
       ***AI***   from HDL.  Moreover, the extent of fusion of the apo
     AII-(53-70)-WT, apo AII-(58-70)-WT and apo AII-(53-70)-30 degrees
       ***peptides***   was related to the alpha-helical content of the
     lipid-bound   ***peptides***   measured by infrared spectroscopy.
     Infrared measurements using polarized light also confirmed the oblique
     orientation of the helical component of the three   ***peptides***   .  In
     native and r-HDL, the tilted insertion of the C-terminal   ***helix***
     of apo AII resulting in a partial destabilization of the HDL external
     lipid layer might contribute to the displacement of   ***apo***
       ***AI***   by apo AII.


=> d his

     (FILE 'HOME' ENTERED AT 19:04:55 ON 08 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     19:05:16 ON 08 JUL 2003
L1             1 S APO-AI AMPHIPATHIC HELIX PEPTIDE
L2          2542 S APO-AI
L3            19 S L2 (P) AMPHIPATHIC (P) PEPTIDE
L4             8 DUPLICATE REMOVE L3 (11 DUPLICATES REMOVED)
L5            21 S L2 (P) HELIX (P) PEPTIDE
```

FILE 'MEDLINE' ENTERED AT 18:35:4[redacted]N 08 JUL 2003

FILE 'CAPLUS' ENTERED AT 18:35:47 ON 08 JUL 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'BIOSIS' ENTERED AT 18:35:47 ON 08 JUL 2003
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FILE 'EMBASE' ENTERED AT 18:35:47 ON 08 JUL 2003
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FILE 'SCISEARCH' ENTERED AT 18:35:47 ON 08 JUL 2003
COPYRIGHT 2003 THOMSON ISI

FILE 'AGRICOLA' ENTERED AT 18:35:47 ON 08 JUL 2003

=> s apolipoprotein A-I
L1 21207 APOLIPOPROTEIN A-I

=> s (fc domain) or (polyethylene glycol) or peg or polylysine or dextran
L2 301385 (FC DOMAIN) OR (POLYETHYLENE GLYCOL) OR PEG OR POLYLYSINE OR DEXTRAN

=> s l1 (p) l2
L3 76 L1 (P) L2

=> s l3 (p) (conjugate or fusion)
L4 2 L3 (P) (CONJUGATE OR FUSION)

=> duplicate remove l4
DUPLICATE PREFERENCE IS 'CAPLUS, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L4
L5 2 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)

=> d l5 1-2 ibib abs

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:514717 CAPLUS
DOCUMENT NUMBER: 127:230065
TITLE: Expression of the human apolipoprotein A-I gene transferred into mammalian cells in vitro and rat liver in vivo
AUTHOR(S): Perevozchikov, A. P.; Dizhe, E. B.; Serov, S. M.; Kuryshev, V. Yu.; Arredouani, M.; Parfenova, N. S.; Shavlovskii, M. M.; Nasonkin, I. O.; Drapchinskaya, N. L.; Bondarev, I. E.; Tsarapkina, E. V.; Sukonina, V. E.; Denisenko, A. D.; Gaitshkoki, V. S.; Klimov, A. N.
CORPORATE SOURCE: Institute of Experimental Medicine, Russian Academy of Medical Sciences, St. Petersburg, 197376, Russia
SOURCE: Molecular Biology (Translation of Molekulyarnaya Biologiya (Moscow)) (1997), 31(2), 178-183
CODEN: MOLBBJ; ISSN: 0026-8933
PUBLISHER: Consultants Bureau
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human apolipoprotein A-I gene (apoA-I) under the control of a potent tissue-nonspecific promoter from the cytomegalovirus early gene or the mouse ribosomal protein L32 gene was transferred into cultured mammalian cells. HeLa cells and rat fibroblasts RAT-1 were transfected with apoA-I-contg. DNA using the calcium phosphate technique and recombinant retroviruses, resp. In both cell cultures, the gene was efficiently expressed in an immunospecific protein product. A complex of apoA-I with a conjugate of poly(L-Lys) and asialic orosomucoid (ASOR) was used to transfect rat liver cells in vivo. Human apolipoprotein A-I (Apo A-I) was detected in rat serum by ELISA 24 h after i.v. injection of the complex. Partial hepatectomy performed 30 min after injecting DNA contg. the lacZ bacterial marker gene promoted its stable (for more than 7 wk) expression in rat liver. Possibilities of using the above methods of gene transfer for efficient stable apoA-I expression in mammalian liver are discussed.

L5 ANSWER 2 OF 2 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 95:437776 SCISEARCH
THE GENUINE ARTICLE: RE377

TITLE: ANTIVIRALS THAT TARGET THE AMINO-TERMINAL DOMAIN OF HIV TYPE-1 GLYCOPROTEIN-41

AUTHOR: GORDON L M (Reprint); WARING A J; CURTAIN C C; KIRKPATRICK A; LEUNG C; FAULL K; MOBLEY P W

CORPORATE SOURCE: UNIV CALIF LOS ANGELES, KING DREW MED CTR, DEPT PEDIAT, MAIL POINT 9, 12021 S WILMINGTON AVE, LOS ANGELES, CA, 90059 (Reprint); MONASH UNIV, DEPT PHYS, CLAYTON, VIC 3052, AUSTRALIA; CSIRO, DIV BIOMOLEC ENGN, PARKVILLE, VIC 3052, AUSTRALIA; UNIV CALIF LOS ANGELES, CTR MOLEC & MED SCI MASS SPECTROMETRY, DEPT CHEM & BIOCHEM, LOS ANGELES, CA, 90024; UNIV CALIF LOS ANGELES, CTR MOLEC & MED SCI MASS SPECTROMETRY, DEPT PSYCHIAT & BIOBEHAV SCI, LOS ANGELES, CA, 90024; CALIF STATE POLYTECH UNIV POMONA, DEPT CHEM, POMONA, CA, 91768

COUNTRY OF AUTHOR: USA; AUSTRALIA

SOURCE: AIDS RESEARCH AND HUMAN RETROVIRUSES, (JUN 1995) Vol. 11, No. 6, pp. 677-686.
ISSN: 0889-2229.

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 47

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Functional and structural studies were made to assess whether a class of antiviral agents targets the N-terminal domain of the glycoprotein 41,000 (gp41) of human immunodeficiency virus type 1 (HIV-1), Previous experiments have shown that the amino-terminal peptide (FP-I; 23 amino acids, residues 519-541) of HIV-1 gp41 is cytolytic to both human erythrocytes (non-CD4(+) cells) and Hut-78 cells (CD4(+) lymphocytes), Accordingly, FP-I-induced hemolysis may be used as a surrogate assay for evaluating the role of the N-terminal gp41 domain in HIV-cell interactions, Here, we studied the blocking of FP-I-induced lysis of erythrocytes by the following anti-HIV agents: (1) IgG [i.e.; anti-(518-541) IgG] raised to an immunoconjugate of Arg-FP-I, (2) apolipoprotein A-1 (ape A-1) and a peptide based on apo A-1, (3) dextran sulfate, (4) gp41 peptide (residues 637-666), and (5) anionic human serum albumins, Dose-response curves indicated that their relative potency in inhibiting FP-I-induced hemolysis was approximately correlated with their previously reported anti-HIV activity, Electron spin resonance (ESR) studies showed that FP-I spin labeled at the N-terminal alanine binds to anti-(518-541) IgG, dextran sulfate, and anionic albumins, The high in vitro antiviral activity and low cytotoxicity of these agents suggest that blocking membrane-FP-I interactions offers a novel approach for AIDS therapy or prophylaxis.

```
=> d his

     (FILE 'HOME' ENTERED AT 18:35:30 ON 08 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     18:35:47 ON 08 JUL 2003
L1         21207 S APOLIPOPROTEIN A-I
L2        301385 S (FC DOMAIN) OR (POLYETHYLENE GLYCOL) OR PEG OR POLYLYSINE OR
L3            76 S L1 (P) L2
L4             2 S L3 (P) (CONJUGATE OR FUSION)
L5             2 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)

=> s l1 (p) (fusion protein)
L6            43 L1 (P) (FUSION PROTEIN)

=> s l1 (p) conjugate
L7            36 L1 (P) CONJUGATE

=> s l6 or l7
L8            79 L6 OR L7

=> duplicate remove l8
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L8
L9             38 DUPLICATE REMOVE L8 (41 DUPLICATES REMOVED)

=> s linker
L10        50011 LINKER

=> s l9 (p) l10
```

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L65 (P) L55'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L69 (P) L57'
L11 0 L9 (P) L10

=> d l9 1-38 ibib abs

L9 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:23439 CAPLUS
DOCUMENT NUMBER: 138:83330
TITLE: APOA1 (apolipoprotein A-I)-interacting proteins, protein complexes, and use thereof
INVENTOR(S): Bartel, Paul; Szankasi, Philippe; Sugiyama, Janice
PATENT ASSIGNEE(S): Myriad Genetics, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp., which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003008373	A1	20030109	US 2002-124767	20020417
PRIORITY APPLN. INFO.:			US 2001-284220P P	20010417
			US 2002-354899P P	20020206

AB Protein complexes are provided comprising APOA1 and one or more APOA1-interacting proteins. The protein complexes are useful in screening assays for identifying compds. effective in modulating the protein complexes and in treating and/or preventing diseases and disorders assocd. with APOA1 and its interacting partners. In addn., methods of detecting the protein complexes and modulating the functions and activities of the protein complexes or interacting members thereof are also provided.

L9 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:150445 CAPLUS
DOCUMENT NUMBER: 138:199935
TITLE: A bifunctional recombinant virus ligand fusion protein containing an antibody binding region and its use for specific cell targeting in gene therapy
INVENTOR(S): Li, Yibing
PATENT ASSIGNEE(S): Rainbow Therapeutic Company, USA
SOURCE: U.S., 24 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6524572	B1	20030225	US 2000-604107	20000626
PRIORITY APPLN. INFO.:			US 2000-604107	20000626

AB Use of recombinant viral vector for gene therapy is hampered by the native virus-host interaction. Non-specific gene transfection causes adverse effects in gene therapy. To solve this problem, a fusion protein ligand capable of modifying viral tropism has been created. The fusion protein comprises a viral cellular receptor at one end and an antibody Fc-binding protein at the other end. By the design, the fusion protein ligand when coupled with an antibody can block the native viral infection and redirect the virus to specific cellular surface marker as long as the antibody binds to this marker. Using adenovirus and adenoviral receptor as an example, the fusion protein ligand when coupled with anti ICAM-1 IgG redirects virus to cultured human endothelial cells expressing ICAM-1. Infection by viruses depends on the presence of viral receptor on the host cells and this requirement limits the use of viral vector for gene therapy. IN particular, a fusion ligand protein comprising coxsackievirus/adenovirus receptor (CAR), and the antibody Fc-binding domain from protein A linked with mouse Ig hinge region is prepd. From in vitro testing, this fusion protein ligand blocks viral gene transduction and, when coupled with anti-ICAM-1 IgG, redirects AdV to endothelial cells that are induced to express ICAM-1. Because the protein A Fc-binding domain will bind to any Ig, the current strategy can be adapted to target a wide variety of tissues or cells as long as an antibody species that recognizes a membrane marker on target tissue or cell is present. This concept may be further expanded to other viruses that employ peptide

receptors. These membrane receptors can be fused to the Fc-binding domain to create a variety of bifunctional ligands for targeting recombinant viruses in gene therapy. The current invention circumvents this requirement, broadens the spectrum of diseases amenable to gene therapy using viral vectors, enhances the viral transfection efficiency in cells or tissues that are refractory to these viruses, and finally provides a safer and more flexible system for gene targeting.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:102770 CAPLUS
DOCUMENT NUMBER: 138:147995
TITLE: Insulin Induction of Apolipoprotein AI, Role of Sp1
AUTHOR(S): Lam, Johnny K.; Matsubara, Shuji; Mihara, Koichiro; Zheng, Xi-long; Mooradian, Arshag D.; Wong, Norman C. W.
CORPORATE SOURCE: Endocrine research group Departments of Medicine and Biochemistry Molecular Biology the Faculty of Medicine, University of Calgary, Calgary, AB, T2N 4N1, Can.
SOURCE: Biochemistry (2003), 42(9), 2680-2690
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Apolipoprotein AI (apo AI) is the major protein component of serum high-d. lipoproteins. The abundance of apo AI correlates inversely with the risk of ischemic heart disease (IHD) and thus enhanced expression of the protein is expected to reduce the risk of IHD. Our previous studies show that insulin enhances apo AI promoter activity and this action requires the GC-rich insulin response core element (IRCE, -411 to -404). The motif binds to a ubiquitous transcription factor Sp1. We have extended studies that examine insulin induction of apo AI using a 41 bp (-425 to -385) fragment of apo AI DNA linked to the trout metallothionein TATA box and fused to luciferase (pIRCE-Luc). Luc activity in Hep G2 cells transfected with pIRCE-Luc was stimulated by insulin, an insulin mimetic bisperoxo (1,10-phenanthroline) oxovanadate (bpv) and the phorbol ester (PDBu). Our previous studies showed that insulin action on apo AI gene transcription flowed down two signaling pathways: Ras-raf and PI3K, leading to activation of the MAPK and PKC kinases, resp. In contrast, PDBu activates only the PKC pathway. Although insulin and PDBu activation of apo AI were distinct, the cascades involved all appeared to target Sp1. Furthermore, exposure of transfected cells to okadaic acid or a phosphatase inhibitor also increased Luc activity and suggested a potential role for phosphorylation, likely involving Sp1. If true, then changes in the IRCE binding activity of Sp1 should be detected following exposure to MAPK, PKC, or the protein phosphatase I (PPI) alone and in various combinations followed by assaying the ability of Sp1 to bind the IRCE. Sp1 binding activity increased with either MAPK or PKC. Although exposure to PPI also affected IRCE binding activity of Sp1, whether it increased or decreased was dependent on the order of exposure to the protein. In summary, the IRCE alone can mediate the stimulatory effects of insulin, bpv, and PDBu, and Sp1 enhances these responses that may arise from phosphorylation of the protein.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 38 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2003245286 IN-PROCESS
DOCUMENT NUMBER: 22652973 PubMed ID: 12754494
TITLE: The C-terminal domain of apolipoprotein A-I contains a lipid-sensitive conformational trigger.
AUTHOR: Oda Michael N; Forte Trudy M; Ryan Robert O; Voss John C
CORPORATE SOURCE: Children's Hospital Oakland Research Institute, Oakland, California 94609-1673, USA.
SOURCE: NATURE STRUCTURAL BIOLOGY, (2003 Jun) 10 (6) 455-60.
Journal code: 9421566. ISSN: 1072-8368.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030528
Last Updated on STN: 20030528
AB Exchangeable apolipoproteins can convert between lipid-free and lipid-associated states. The C-terminal domain of human ***apolipoprotein*** ***A*** - ***I*** (apoA-I) plays a role in

both lipid binding and self-association. Site-directed spin-label electron paramagnetic resonance spectroscopy was used to examine the structure of the apoA-I C terminus in lipid-free and lipid-associated states. Nitroxide spin-labels positioned at defined locations throughout the C terminus were used to define discrete secondary structural elements. Magnetic interactions between probes localized at positions 163, 217 and 226 in singly and doubly labeled apoA-I gave inter- and intramolecular distance information, providing a basis for mapping apoA-I tertiary and quaternary structure. Spectra of apoA-I in reconstituted HDL revealed a lipid-induced transition of defined random coils and beta-strands into alpha-helices. This conformational switch is analogous to triggered events in viral ***fusion*** ***proteins*** and may serve as a means to overcome the energy barriers of lipid sequestration, a critical step in cholesterol efflux and HDL assembly.

L9 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:408803 CAPLUS
DOCUMENT NUMBER: 137:1503
TITLE: Fusion protein of immunoglobulin heavy chain constant region and .beta.-amyloid fragment as therapeutic agent for Alzheimer's disease
INVENTOR(S): Gefter, Malcolm L.; Israel, David I.; Joyal, John L.; Gosselin, Michael
PATENT ASSIGNEE(S): Praecis Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042462	A2	20020530	WO 2001-US44581	20011127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002025772	A5	20020603	AU 2002-25772	20011127
US 2002133001	A1	20020919	US 2001-996357	20011127

PRIORITY APPLN. INFO.:
US 2000-253302P P 20001127
US 2000-250198P P 20001129
US 2000-257186P P 20001220
WO 2001-US44581 W 20011127

AB The present invention provides therapeutic agents and methods of use thereof for treating an amyloidogenic disease, e.g., Alzheimer's disease. The therapeutic agents of the invention include compds. comprising the formula I-L-P, wherein I is an Ig heavy chain const. region or fragment thereof (e.g., comprising the Fc region); L is a linker group or a direct bond; and P is a peptide capable of binding an amyloidogenic protein. It is believed that the P portion of the compds. of the invention will serve to bind an amyloidogenic protein, e.g., an amyloidogenic protein within an amyloid plaque, and the I portion of the compds. of the invention will serve to direct microglia to the amyloidogenic protein, which microglia may then internalize and degrade the amyloidogenic protein and the amyloid plaque. COS cells were transfected with DNA encoding various segments of .beta.-amyloid flanked by the mouse IgGI Fc region. COS cells expressing the Fc Region of mouse IgG1 fused to amino acid residues 1-40, 1-42, 10-25, 16-30, 17-21, or 17-21-(A21L) of .beta.-amyloid with or without an N-terminal triple glycine cap were resolved by SDS-PAGE in the absence of a reducing agent and examd. by Western blot anal. The ability of a compd. of the invention to modulate (e.g., inhibit or promote) the aggregation of natural .beta.-AP when combined with the natural .beta.-AP was examd. using the Fibril binding assay. The results from this expt. (set forth in Figure 9), demonstrate that the compds. tested [e.g., PPI-1019, PPI-1621 and three different prepns. of A.beta.(16-30)-Fc] are effective inhibitors of A.beta. aggregation. The ability of A.beta.(16-30)-Fc to clear amyloid plaques in a mouse model of Alzheimer's disease was assessed. The fusion protein was administered to a mouse transgenic for both the Swedish mutation of amyloid precursor protein and presenilin M146L by direct infusion into the cerebral cortex in one hemisphere. As indicated in Figure 10, the plaque burden at the site of infusion was significantly

decreased compared to the controlled hemisphere.

L9 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:368513 CAPLUS
DOCUMENT NUMBER: 136:380110
TITLE: Apolipoprotein A analogs capable of forming HDL and with extended serum half-lives and stronger binding to cubilin for treatment of cardiovascular disease
INVENTOR(S): Graversen, Jonas; Moestrup, Soren
PATENT ASSIGNEE(S): Proteopharma Aps, Den.
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038609	A2	20020516	WO 2001-DK739	20011109
WO 2002038609	A3	20020926		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002013843	A5	20020521	AU 2002-13843	20011109
US 2002156007	A1	20021024	US 2001-987107	20011113

PRIORITY APPLN. INFO.:

DK 2000-1682	A	20001110
DK 2001-57	A	20010115
US 2001-264022P	P	20010126
WO 2001-DK739	W	20011109

AB The invention relates to an apolipoprotein construct, an apolipoprotein construct for use as a medicament, a nucleic acid sequence encoding the apolipoprotein construct, a vector comprising the nucleic acid sequence, a method for producing the apolipoprotein construct, and use of the apolipoprotein construct for the prepn. of apharmaceutical compn. Specifically, analogs and fusion proteins of apolipoprotein AI are described. The presented data document that the constructs according to the invention are capable of binding lipids, are capable of binding cubilin, which is a strong Apo AI receptor, stronger than native Apo A-I and that the plasma half life of the constructs is at least tripled compared to native Apo A-I. Together these data document that the constructs according to the invention are strong candidates for treatment of cardiovascular diseases.

L9 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:730152 CAPLUS
DOCUMENT NUMBER: 138:167274
TITLE: The ABCA1 transporter functions on the basolateral surface of hepatocytes
AUTHOR(S): Neufeld, Edward B.; Demosky, Steven J., Jr.; Stonik, John A.; Combs, Christian; Remaley, Alan T.; Duverger, Nicolas; Santamarina-Fojo, Silvia; Brewer, H. Bryan, Jr.
CORPORATE SOURCE: Molecular Disease Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Biochemical and Biophysical Research Communications (2002), 297(4), 974-979
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ABCA1 transporter on the cell surface and in endosomes plays an essential role in the cell-mediated lipidation of ***apolipoprotein*** ***A*** - ***I*** (apo A-I) to form nascent HDL. The authors' previous studies of transgenic mice overexpressing ABCA1 suggested that ABCA1 in the liver plays a major role in regulating plasma HDL levels. Here, the site of function of ABCA1 in the polarized hepatocyte was assessed by expression of an adenoviral construct encoding a human ABCA1-GFP ***fusion*** ***protein*** in the polarized hepatocyte-like WIF-B cell line.

Consistent with localization of ABCA1 at the basolateral (vascular) cell surface, expression of ABCA1-GFP stimulated apo A-I mediated efflux of WIF-B cell cholesterol into the culture medium. Confocal fluorescence microscopy revealed that ABCA1-GFP was expressed solely on the basolateral surface and assocd. endocytic vesicles. These findings suggest an important role for hepatocyte basolateral membrane ABCA1 in the regulation of the levels of intracellular hepatic cholesterol, as well as plasma HDL.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:629462 CAPLUS
DOCUMENT NUMBER: 138:326394
TITLE: Lipid-drug-conjugate (LDC) nanoparticles as novel carrier system for the hydrophilic antitrypanosomal drug diminazenediaceturate
AUTHOR(S): Olbrich, Carsten; Gessner, Andrea; Kayser, Oliver; Muller, Rainer Helmut
CORPORATE SOURCE: Department of Pharmaceutics, Biopharmaceutics and Biotechnology, The Free University of Berlin, Berlin, D-12169, Germany
SOURCE: Journal of Drug Targeting (2002), 10(5), 387-396
CODEN: JDTAEH; ISSN: 1061-186X
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of the present study was to incorporate the hydrophilic drug diminazene diaceturate at a high loading into lipid nanoparticles by creating nanoparticles from lipid-drug conjugates (LDC). IR and DSC data showed that the antitrypanosomal drug diminazene is able to react with fatty acids to form water-insol. salts like diminazenedistearate and dioleate. The salts could be transformed into nanoparticles using high-pressure homogenization technique, established for solid lipid nanoparticles (SLN). By using polysorbate 80 as surfactant, phys. stable LDC nanoparticle dispersions of both salts could be obtained. The mean PCS diams. and polydispersity indexes were 364 nm and 0.233 for diminazenedistearate and 442 nm and 0.268 for diminazenedioleate, resp. Due to the compn. of the LDC bulk materials, nanoparticles with a high drug load of 33% (wt./wt.) were obtained even for this highly water-sol. drug diminazenediaceturate. The new carrier system of LDC nanoparticles overcomes one limitation of SLN, i.e. the limited loading capacity for hydrophilic drugs. Transforming water-sol. hydrophilic drugs into LDC and formation of nanoparticles allows prolonged drug release and targeting to specific sites by i.v. injection. These results provide a first basis of using LDC-polysorbate 80 nanoparticles for brain delivery of diminazene to treat second stage human African trypanosomiasis (HAT).
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:833532 CAPLUS
DOCUMENT NUMBER: 135:368551
TITLE: Fusion protein approach to improve crystal quality for structure determination by X-ray diffractometry
INVENTOR(S): Iwata, So; Byrne, Bernadette; Jormakka, Mika; Abramson, Jeff; Sejlitz, Torsten
PATENT ASSIGNEE(S): Imperial College Innovations Limited, UK
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085962	A1	20011115	WO 2001-GB2043	20010504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1278875	A1	20030129	EP 2001-929794	20010504

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: SE 2000-1666 A 20000505
US 2000-209331P P 20000602
SE 2000-2432 A 20000628
WO 2001-GB2043 W 20010504

AB A method of improving the quality of crystals of proteins by manufg. them as fusion products with a protein which, when crystd. with a second protein, is capable of accommodating the second protein in the crystal lattice. Expression vectors for the manuf. of these fusion proteins are described. The invention further provides a recombinant vector comprising (i) a promoter sequence and (ii) a nucleotide sequence encoding a first protein which upon crystn. yields crystals having available space in the lattice, so as to allow for the ordered packing of a second protein into the said available space, said recombinant vector further allowing, for the insertion of a further nucleotide sequence encoding a second protein to be accommodated, upon its crystn., in the said available space in the lattice of the first protein.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:693510 CAPLUS
DOCUMENT NUMBER: 135:271905
TITLE: Apolipoprotein A-I and its fragments regulate T-cell-dependent monocyte activation
INVENTOR(S): Edwards, Carl K., III; Burger, Danielle; Dayer, Jean-Michel; Kohno, Tadahiko
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068852	A2	20010920	WO 2001-US7826	20010313
WO 2001068852	A3	20020228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002064820	A1	20020530	US 2001-803918	20010313
EP 1268782	A2	20030102	EP 2001-918561	20010313

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-189008P P 20000313
US 2000-193551P P 20000331
WO 2001-US7826 W 20010313

AB The invention provides apolipoprotein A-I fragment T cell activation inhibitor (AFTI) polypeptides and nucleic acid mols. encoding the same. Apolipoprotein and its fragments are shown to regulate T-cell mediated activation of monocytes via the inhibition of interleukin-1.beta. and tumor necrosis factor-.alpha. secretion. A fragment of apo-A-I comprising domains II and III also displays inhibitory activity. The invention also provides vectors, host cells, selective binding agents, and methods for producing AFTI polypeptides. Also provided are methods for the treatment, diagnosis, amelioration, or prevention of diseases with AFTI polypeptides, particularly IL-1 mediated diseases, TNF-.alpha. mediated diseases, and diseases involving monocyte activation.

L9 ANSWER 11 OF 38 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001161035 MEDLINE
DOCUMENT NUMBER: 21159106 PubMed ID: 11258924
TITLE: Characterization of the maturation of human pro-apolipoprotein A-I in an in vitro model.
AUTHOR: Pyle L E; Sviridov D; Fidge N H
CORPORATE SOURCE: Baker Medical Research Institute, Melbourne, Victoria, 3008, Australia.
SOURCE: BIOCHEMISTRY, (2001 Mar 13) 40 (10) 3101-8.

Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010503

AB The reaction conditions and the protein structural features involved in the maturation of pro- ***apolipoprotein*** ***A*** - ***I*** (cleavage of pro-peptide) were investigated in an in vitro model. ProapoA-I, mutants and wild type, were expressed in the PGEX/E. coli expression system as ***fusion*** ***proteins*** with glutathione S-transferase (GST). Use of GST-proapoA-I and truncated forms of proapoA-I enabled quantitation of the amount of GST and apoA-I formed as a result of cleavage following incubation with human serum. Deletion of the pro-peptide (GST-apoA-I) resulted in complete inhibition of the reaction. Truncation of proapoA-I to residues 222, 150, 135, and 25 as well as substitution of residues -6, -5, and -4 with alanine did not affect the reaction. Substitution of residues -1, -2, 1, 3, and 4 with alanine either completely blocked or substantially inhibited cleavage of the pro-peptide. The reaction was inhibited by addition of EDTA, o-phenanthroline, dithiothreitol, and beta-mercaptoethanol and to a lesser extent by p-chloromercuriphenylsulfonic acid, but not by leupeptin, N-ethylmaleimide, PMSF, pepstatin A, or trans-epoxysuccinyl-L-leucylamido(4-guanidino)butane. Calcium was essential for the activation of the cleavage enzyme, but it had a biphasic effect on the cleavage, activating it at concentrations below 1.5 mM and inhibiting at concentrations above 1.75 mM. Manganese alone was not essential for activation of the enzyme nor did it modify the effect of low concentration of calcium. However, a high concentration of manganese partially reverted the inhibitory effect of a high calcium concentration. Thus, residues within -2 to +4 are involved in forming the cleavage site for the maturation enzyme. The reaction of maturation is inhibited by metalloprotease inhibitors and is dependent upon calcium.

L9 ANSWER 12 OF 38 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001688474 MEDLINE
DOCUMENT NUMBER: 21592544 PubMed ID: 11734582
TITLE: Preparation and incorporation of probe-labeled apoA-I for fluorescence resonance energy transfer studies of rHDL.
AUTHOR: Li H H; Thomas M J; Pan W; Alexander E; Samuel M; Sorci-Thomas M G
CORPORATE SOURCE: Department of Pathology, The Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA.
CONTRACT NUMBER: HL49373 (NHLBI)
HL60079 (NHLBI)
HL64163 (NHLBI)
HL64963 (NHLBI)
SOURCE: JOURNAL OF LIPID RESEARCH, (2001 Dec) 42 (12) 2084-91.
Journal code: 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20011206
Last Updated on STN: 20030316
Entered Medline: 20020305

AB ***Apolipoprotein*** ***A*** - ***I*** (apoA-I), the major constituent of HDL, plays an essential role in regulating cholesterol metabolism, acting as the physiological activator of lecithin: cholesterol acyltransferase, which converts cholesterol to cholesterol ester. Thiol-reactive fluorescent probes attached to cysteine-containing apoA-I mutants are currently being used to investigate the "LCAT active" conformation of lipid-bound apoA-I. Herein, we report new methodologies allowing rapid expression, fluorescent labeling, and recombinant HDL (rHDL) preparation for use in apoA-I in fluorescence resonance energy transfer (FRET) studies. Cysteine-containing mutant forms of human apoA-I were cloned into the pTYB12 vector containing a T7 promoter, a modified self-splicing protein element (intein), and a small affinity tag [chitin binding domain (CBD)]. The ***fusion*** ***proteins*** were expressed in Escherichia coli, isolated from cell lysates, and bound to a chitin-affinity column. Release of mature human apoA-I was initiated by the addition of DTT, which induced self-cleavage at the COOH terminus of

the intein - CBD ***fusion*** ***protein*** . ApoA-I was further purified by Q-sepharose and [redacted] used for fluorescent probe [redacted]ling. Discoidal rHDL were then prepared with donor and/or acceptor labeled apoA-I and characterized with respect to their size, composition and ability to activate LCAT.

L9 ANSWER 13 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:173686 BIOSIS
DOCUMENT NUMBER: PREV200100173686
TITLE: Apolipoprotein specificity for lipid efflux by the human ABCAI transporter.
AUTHOR(S): Remaley, Alan T. (1); Stonik, John A.; Demosky, Steven J.; Neufeld, Edward B.; Bocharov, Alexander V.; Vishnyakova, Tatyana G.; Eggerman, Thomas L.; Patterson, Amy P.; Duverger, Nicholas J.; Santamarina-Fojo, Silvia; Brewer, H. Bryan, Jr.
CORPORATE SOURCE: (1) NHLBI, National Institutes of Health, 10 Center Drive, Bldg. 10/7N115, Bethesda, MD, 20892: aremaley@nih.gov USA
SOURCE: Biochemical and Biophysical Research Communications, (January 26, 2001) Vol. 280, No. 3, pp. 818-823. print. ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB ABCAI, a member of the ATP binding cassette family, mediates the efflux of excess cellular lipid to HDL and is defective in Tangier disease. The apolipoprotein acceptor specificity for lipid efflux by ABCAI was examined in stably transfected Hela cells, expressing a human ABCAI-GFP fusion protein. ApoA-I and all of the other exchangeable apolipoproteins tested (apoA-II, apoA-IV, apoC-I, apoC-II, apoC-III, apoE) showed greater than a threefold increase in cholesterol and phospholipid efflux from ABCAI-GFP transfected cells compared to control cells. Expression of ABCAI in Hela cells also resulted in a marked increase in specific binding of both apoA-I (Kd = 0.60 mug/mL) and apoA-II (Kd = 0.58 mug/mL) to a common binding site. In summary, ABCAI-mediated cellular binding of apolipoproteins and lipid efflux is not specific for only apoA-I but can also occur with other apolipoproteins that contain multiple amphipathic helical domains.

L9 ANSWER 14 OF 38 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001270112 MEDLINE
DOCUMENT NUMBER: 21154125 PubMed ID: 11254750
TITLE: Role of individual amino acids of apolipoprotein A-I in the activation of lecithin:cholesterol acyltransferase and in HDL rearrangements.
AUTHOR: Cho K H; Durbin D M; Jonas A
CORPORATE SOURCE: Department of Biochemistry, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA.
CONTRACT NUMBER: HL-16059 (NHLBI)
HL-29939 (NHLBI)
SOURCE: JOURNAL OF LIPID RESEARCH, (2001 Mar) 42 (3) 379-89. Journal code: 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010521
AB The central region of ***apolipoprotein*** ***A*** - ***I*** (apoA-I), spanning residues 143--165, has been implicated in lecithin:cholesterol acyltransferase (LCAT) activation and also in high density lipoprotein (HDL) structural rearrangements. To examine the role of individual amino acids in these functions, we constructed, overexpressed, and purified two additional point mutants of apoA-I (P143R and R160L) and compared them with the previously studied V156E mutant. These mutants have been reported to occur naturally and to affect HDL cholesterol levels and cholesterol esterification in plasma. The P143R and R160L mutants were effectively expressed in Escherichia coli as ***fusion*** ***proteins*** and were isolated in at least 95% purity. In the lipid-free state, the mutants self-associated similarly to wild-type protein. All the mutants, including V156E, were able to lyse dimyristoylphosphatidylcholine liposomes. In the lipid-bound state, the major reconstituted HDL (rHDL) of the mutants had diameters similar to wild type (96--98 A). Circular dichroism and fluorescence methods revealed no major differences among the structures of the lipid-free or

lipid-bound mutants and wild type. In contrast, the V156E mutant had exhibited significant structural, stability, and self-association differences compared with wild-type apoA-I in the lipid-free state, and formed rHDL particles with larger diameters. In this study, limited proteolytic digestion with chymotrypsin showed that the V156E mutant, in lipid-free form, has a distinct digestion pattern and surface exposure of the central region, compared with wild type and the other mutants. Reactivity of rHDL with LCAT was highest for wild type (100%), followed by P143R (39%) and R160L (0.6%). Tested for their ability to rearrange into 78-A particles, the rHDL of the two mutants (P143R and R160L) behaved normally, compared with the rHDL of V156E, which showed no rearrangement after the 24-h incubation with low density lipoprotein (LDL). Similarly, the rHDL of V156E was resistant to rearrangement in the presence of apoA-I or apoA-II. These results indicate that structural changes are absent or modest for the P143R and R160L mutants, especially in rHDL form; that these mutants have normal conformational adaptability; and that LCAT activation is obliterated for R160L.Thus, individual amino acid changes may have markedly different structural and functional consequences in the 143--165 region of apoA-I. The R160L mutation appears to have a direct effect in LCAT activation, while the P143R mutation results in only minor structural and functional effects. Also, the processes for LCAT activation and hinge mobility appear to be distinct even if the same region of apoA-I is involved. -- Cho, K-H., D. M. Durbin, and A. Jonas. Role of individual amino acids of ***apolipoprotein*** ***A*** - ***I*** in the activation of lecithin:cholesterol acyltransferase and in HDL rearrangements. J. Lipid Res. 2001. 42: 379--389.

L9 ANSWER 15 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2001:936413 SCISEARCH
THE GENUINE ARTICLE: 487UW
TITLE: ***Apolipoprotein*** ***A*** - ***I*** interaction with lipid induces a conformational transition analogous to that of viral ***fusion*** ***proteins***
AUTHOR: Oda M N (Reprint); Voss J C; Ryan R O; Forte T M
CORPORATE SOURCE: Childrens Hosp, Oakland, CA 94609 USA; Univ Calif Davis, Davis, CA 95616 USA; Univ Calif Berkeley, Lawrence Berkeley Lab, Berkeley, CA 94720 USA
COUNTRY OF AUTHOR: USA
SOURCE: CIRCULATION, (23 OCT 2001) Vol. 104, No. 17, Supp. [S], pp. 211-211. MA 1016.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA.
ISSN: 0009-7322.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L9 ANSWER 16 OF 38 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001245800 MEDLINE
DOCUMENT NUMBER: 21180317 PubMed ID: 11282243
TITLE: The role of plasma proteins in brain targeting: species dependent protein adsorption patterns on brain-specific lipid drug conjugate (LDC) nanoparticles.
AUTHOR: Gessner A; Olbrich C; Schroder W; Kayser O; Muller R H
CORPORATE SOURCE: Department of Pharmaceutics, Biopharmaceutics and Biotechnologie, Free University of Berlin, Kelchstr. 31, D-12169 Berlin, Germany.
SOURCE: INTERNATIONAL JOURNAL OF PHARMACEUTICS, (2001 Feb 19) 214 (1-2) 87-91.
Journal code: 7804127. ISSN: 0378-5173.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB The in vivo organ distribution of particulate drug carriers is decisively influenced by the interaction with plasma proteins after i.v. administration. Serum protein adsorption on lipid drug ***conjugate*** nanoparticles, a new carrier system for i.v. application, was investigated by 2-dimensional electrophoresis (2-DE). The particles were surface-modified to target them to the brain. To assess the protein adsorption pattern after i.v. injection in mice prior to in vivo studies, the particles were incubated in mouse serum. Incubation in human serum

was carried out in parallel to investigate similarities or differences in the protein patterns obtained from men and mice. Distinct differences were found. Particles incubated in human serum showed preferential adsorption of ***apolipoproteins*** ***A*** - ***I*** , A-IV and E. Previously, preferential adsorption of ApoE was reported as one important factor for targeting of Tween(R)80 modified polybutylcyanoacrylate nanoparticles to the brain. Preferential adsorption of ApoA-I and A-IV took place after incubation in mouse serum, adsorption of ApoE could not be clearly confirmed. In vivo localization of the LDC nanoparticles at the blood-brain barrier and diffusion of the marker Nile Red into the brain could be shown by confocal laser-scanning microscopy. Differences of the obtained adsorption patterns are discussed with regard to their relevance for correlations of in vitro and in vivo data obtained from different species.

L9 ANSWER 17 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:264047 BIOSIS
DOCUMENT NUMBER: PREV200200264047
TITLE: ***Apolipoprotein*** ***A*** - ***I*** interaction with lipid induces a conformational transition analogous to that of viral ***fusion*** ***proteins*** .
AUTHOR(S): Oda, Michael N. (1); Voss, John C.; Ryan, Robert O.; Forte, Trudy M.
CORPORATE SOURCE: (1) Children's Hosp, Oakland, CA USA
SOURCE: Circulation, (October 23, 2001) Vol. 104, No. 17 Supplement, pp. II.211. http://circ.ahajournals.org/. print.
Meeting Info.: Scientific Sessions 2001 of the American Heart Association Anaheim, California, USA November 11-14, 2001
ISSN: 0009-7322.
DOCUMENT TYPE: Conference
LANGUAGE: English

L9 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:307119 CAPLUS
DOCUMENT NUMBER: 132:318588
TITLE: Retroviral vector targeted to specific cell-types mediated by a soluble retroviral receptor-ligand fusion protein
INVENTOR(S): Young, John A. T.; Mulligan, Richard C.; Snitkovsky, Sophie; Niederman, Thomas M. J.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA; The Children's Medical Center Corp.
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6060316	A	20000509	US 1999-327841	19990608

PRIORITY APPLN. INFO.: US 1998-88622P P 19980609
AB A sol. retroviral receptor-ligand fusion protein is used to mediate retroviral vector's specific cell-type targeting. The sol. viral receptor moiety of the above fusion mols. binds to the viral envelope protein and its ligand moiety binds to a cell-type specific cellular receptor; these interaction can bring virions and target cells sufficiently close and activate viral entry and infection. The sol. retroviral receptor-ligand fusion mols. can be incorporated onto virus particles or directly conjugated to the surface of virions. This method can increase the viral infectivity and specificity and may be applied to specific gene delivery for gene therapy.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:672002 CAPLUS
DOCUMENT NUMBER: 133:340063
TITLE: Serum protein adsorption on lipid drug conjugate-nanoparticles (LDC-NP): Evaluation by two-dimensional electrophoresis
AUTHOR(S): Gessner, A.; Olbrich, C.; Kayser, O.; Muller, R. H.
CORPORATE SOURCE: Department of Pharmaceutics, Biopharmaceutics and

Biotechnology, The Free University, Berlin, Germany
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (2000), 27th, 301-302
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two-dimensional electrophoresis (2-DE) was previously established to analyze plasma or serum protein adsorption patterns on different carrier systems, e.g. polymeric particles or emulsions. Selected results of the first protein adsorption studies on LDC-Nanoparticles (Np) for potential i.v. application by 2-DE were presented.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2000:355548 SCISEARCH
THE GENUINE ARTICLE: 310RV
TITLE: Tilted peptides: a motif for membrane destabilization (hypothesis)
AUTHOR: Brasseur R (Reprint)
CORPORATE SOURCE: FAC UNIV SCI AGRON GEMBLOUX, CTR BIOPHYS MOL NUMER, PASSAGE DEPORTES 2, B-5030 GEMBLOUX, BELGIUM (Reprint)
COUNTRY OF AUTHOR: BELGIUM
SOURCE: MOLECULAR MEMBRANE BIOLOGY, (JAN-MAR 2000) Vol. 17, No. 1, pp. 31-40.
Publisher: TAYLOR & FRANCIS LTD, 11 NEW FETTER LANE, LONDON EC4P 4EE, ENGLAND.
ISSN: 0968-7688.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 77
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Cell life depends on the dynamics of molecular processes: molecule folding, organelle building and transformations involving membrane fusion, protein activation and degradation. To carry out these processes, the hydrophilic/hydrophobic interfaces of amphipathic systems such as membranes and native proteins must be disrupted. In the past decade, protein fragments acting in the disruption of interfaces have been evidenced: they are named the tilted or oblique peptides. Due to a peculiar distribution of hydrophobicity, they can disrupt hydrophobicity interfaces. Tilted peptides should be present in many proteins involved in various stages of cell life. This hypothesis overviews their discovery, describes how they are detected and discusses how they could be involved in dynamic biological processes.

L9 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:113797 CAPLUS
DOCUMENT NUMBER: 130:166800
TITLE: Soluble fusion proteins of aggregate-forming proteins and the study of diseases associated with protein aggregate formation
INVENTOR(S): Wanker, Erich; Lehrach, Hans; Scherzinger, Eberhard; Bates, Gillian
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Forderung der Wissenschaften e.V., Germany
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906545	A2	19990211	WO 1998-EP4811	19980731
WO 9906545	A3	19990805		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1001987	A2	20000524	EP 1998-945134	19980731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: EP 1997-113306 19970801
WO 1998-EP4811 19980731

AB Fusion proteins of aggregate-forming proteins and solubilizing peptides are described for use in elucidating the mechanism, onset or progress of diseases assocd. with the formation of amyloid-like fibrils or protein aggregates. The method is for use in the study of neurol. diseases such as Huntington's and Alzheimer's. The fusion proteins can also be used to screen for inhibitors of aggregation that may be of therapeutic use. Genes for a series of fusion proteins polyglutamine repeat expansion variants (20, 30, or 51 glutamine repeats) of huntingtin and glutathione-S-transferase were constructed by std. methods and manufd. in Escherichia coli using a hexahistidine for affinity purifn. The fusion proteins were sol. but cleavage of the 51 glutamine repeat variant (HD51) with trypsin led to the formation of insol. aggregates of the huntingtin. HD51 aggregated in vitro to form amyloid-like birefringent fibrils after liberation by trypsin cleavage, but the shorter repeat variants HD20 and HD30 did not do so. Similar effects were seen in vivo in COS-1 cells.

L9 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:761517 CAPLUS
DOCUMENT NUMBER: 131:347085
TITLE: Effects of 17.alpha.-dihydroequilenin on plasma lipid and lipoprotein, glucose, insulin concentrations, coronary artery vasomotor function, and reproductive organ and mammary gland proliferation in atherosclerotic mammals
INVENTOR(S): Washburn, Scott A.; Clarkson, Thomas B.; Adams, Michael R.; Register, Thomas C.; Williams, J. Koudy; Wagner, Janice D.; Cline, J. Mark; Adelman, Steven J.
PATENT ASSIGNEE(S): Wake Forest University, USA; American Home Products Corporation
SOURCE: U.S., 14 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5994337	A	19991130	US 1998-6000	19980112
US 6147069	A	20001114	US 1999-391985	19990909
US 6207659	B1	20010327	US 1999-392191	19990909

PRIORITY APPLN. INFO.: US 1997-34495P P 19970113
US 1998-6000 A3 19980112

AB The present invention relates to a method of using 17.alpha.-dihydroequilenin and metabolic ***conjugates*** thereof to prevent and reduce atherogenesis in males and females without causing endometrial proliferation in females and without producing feminizing changes in males. 17.alpha.-Dihydroequilenin was evaluated for its effects on plasma lipid and lipoprotein, glucose, insulin concns., coronary artery vasomotor function, and reproductive organ and mammary gland proliferation in atherosclerotic mammals. 17.alpha.-Dihydroequilenin was found to prevent endothelium-dependent vasoconstriction in males ($p<0.05$) and ovariectomized females ($p<0.08$). 17.alpha.-Dihydroequilenin treatment increased plasma ***apolipoprotein*** ***A*** - ***I*** concns. ($p<0.05$) and lowered fasting insulin concns. ($p<0.05$) without changing fasting plasma glucose concns. in males. 17.alpha.-Dihydroequilenin had no other effects on plasma lipid and lipoprotein concns. in either males or females. Also, 17.alpha.-dihydroequilenin exhibited no trophic effects on the uterus, endometrium, or breast, and no effect on either prostatic or testicular wt. Thus, 17.alpha.-dihydroequilenin may prevent breast and prostatic hyperplasia and neoplasia, and has no feminizing effects on the male urogenital system or mammary gland.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:608328 CAPLUS
TITLE: Papers to Appear in Forthcoming Issues
AUTHOR(S): Anon.
SOURCE: Protein Expression and Purification (1999), 17(1), iv
CODEN: PEXPEJ; ISSN: 1046-5928
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; Miscellaneous
LANGUAGE: English
AB Heterologous Gene Expression in a Membrane-Protein-Specific System George J. Turner, Regina Reusch, Ann M. Winter-Vann, Lynell Martinez, and Mary C. Betlach Expression, Purifn., and Structural Characterization of the

Bacteriorhodopsin-Aspartyl T[redacted]scarbamylase ***Fusion*** ***Protein*** George J. [redacted]ner, Larry J. W. Miercke, Alok[redacted] Mitra, Robert M. Stroud, Mary C. Betlach, and Ann Winter-Vann Effectivity of Expression of Mature Forms of Mutant Human ***Apolipoprotein*** ***A*** - ***I*** Dmitri Sviridov, Anh Luong, Louise Pyle, and Noel Fidge Introduction of Protein Kinase Recognition Sites into Proteins: A Review of Their Prepn., Advantages, and Applications Sidney Pestka, Lei Lin, Wei Wu, and Lara Izotova Effect of the Codon Following the ATG Start Site on the Expression of Ovine Growth Hormone in Escherichia coli Niti Puri, K. B. C. Appa Rao, Swapna Menon, A. K. Panda, Gunjan Tiwari, L. C. Garg, and S. M. Totey Large-Scale Expression and Purifn. of a Sol. Form of the Pleckstrin Homol. Domain of the Human Protooncogenic Serine/Threonine Protein Kinase PKB (c-Akt) in Escherichia coli Evan Ingley and Brian A. Hemmings Matrix-Assisted Refolding of Single-Chain Fv-Cellulose Binding Domain ***Fusion*** ***Proteins*** Yevgeny Berdichevsky, Raphael Lamed, Dan Frenkel, Uri Gophna, Edward A. Bayer, Sima Yaron, Yuval Shoham, and Itai Benhar.

L9 ANSWER 24 OF 38 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97443397 MEDLINE
DOCUMENT NUMBER: 97443397 PubMed ID: 9298258
TITLE: Immortalized human hepatocytes as a tool for the study of hepatocytic (de-)differentiation.
AUTHOR: Schippers I J; Moshage H; Roelofsen H; Muller M; Heymans H S; Ruiters M; Kuipers F
CORPORATE SOURCE: Department of Pediatrics, University Hospital Groningen, The Netherlands.
SOURCE: CELL BIOLOGY AND TOXICOLOGY, (1997 Jul) 13 (4-5) 375-86. Journal code: 8506639. ISSN: 0742-2091.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980116
Last Updated on STN: 20020919
Entered Medline: 19971224

AB Primary human hepatocytes were immortalized by stable transfection with a recombinant plasmid containing the early region of simian virus (SV) 40. The cells were cultured in serum-free, hormonally defined medium during the immortalization procedure. Foci of dividing cells were seen after 3 months. Albumin- and fibrinogen-secreting cells were selected and cloned by limiting dilution to obtain homologous cell populations. The established IHH (immortalized human hepatocyte) cell lines were evaluated for their usefulness in studying the regulation of cell growth and of certain differentiated hepatocyte functions. IHH cells retain several differentiated features of normal hepatocytes. They display albumin secretion at a level comparable to cultured primary human hepatocytes (30 micrograms albumin/ml per day). A portion of the IHH cells are polarized, forming bile canaliculi-like vacuoles where exogeneous organic anions accumulate. The multidrug resistance (MDR) P-glycoprotein, known to be localized at the canalicular membrane, is also present in these vacuoles. The polarized features allowed the use of IHH cells for the study of localization of the newly characterized multidrug resistance protein MRP1. The homologues of MRP were found in hepatocytes, MRP1 and MRP2 (cMOAT), both functioning in ATP-dependent excretion of anionic ***conjugates*** . In differentiated hepatocytes, MRP1 expression is extremely low. In contrast, MRP1 is highly expressed in proliferating IHH cells, where it is localized in lateral membranes. A highly differentiated feature of short-term cultured primary hepatocytes which is not detectable in IHH cells is active uptake of the bile salt taurocholate. Furthermore, IHH cells secrete triglyceride (TG)-rich lipoproteins, apolipoprotein B (0.6 microgram/ml per day), and ***apolipoprotein*** ***A*** - ***I*** (1 microgram/ml per day). However, they secrete apoB-containing TG-rich lipoproteins mainly in the LDL density range, while short-term cultured primary hepatocytes mainly secrete TG-rich lipoproteins in the VLDL density range. In conclusion, functions that are rapidly lost in short-term hepatocyte cultures are, in general, not displayed by IHH cells. Immortalized human hepatocytes provide a valuable tool for studying the regulation of hepatocyte proliferation-related phenomena.

L9 ANSWER 25 OF 38 BIOSIS
ACCESSION NUMBER: 1997:344867 BIOSIS
DOCUMENT NUMBER: PREV199799644070
TITLE: Expression of human apolipoprotein A-I gene transferred in vitro into mammalian cells and in vivo into rat liver.
AUTHOR(S): Perevozchikov, A. P. (1); Dizhe, E. B.; Serov, S. M.;

Kuryshev, V. Y[illegible]; Arredouani, M.; Parfenova, N. S.; Shavlovskii, [illegible].; Nasonkin, I. O.; Drapchins[illegible]a, N. L.; Bondarev, I. E.; Tsarapkina, E. V.; Sukonina, V[illegible] E.; Denisenko, A. D.; Gaitskhoki, V. S.; Klimov, A. N.
CORPORATE SOURCE: (1) Inst. Exp. Med., Russ. Acad. Med. Sci., St. Petersburg 197376 Russia
SOURCE: Molekulyarnaya Biologiya (Moscow), (1997) Vol. 31, No. 2, pp. 216-223.
ISSN: 0026-8984.
DOCUMENT TYPE: Article
LANGUAGE: Russian
SUMMARY LANGUAGE: Russian
AB Genetic constructions containing human ***apolipoprotein*** ***A*** - ***I*** gene (apoA-1) controlled by strong tissue-nonspecific promoters (early cytomegalovirus gene, murine ribosomal protein L32) were used to transfer apoA-I gene into cultured mammalian cells. After calcium-phosphate transformation of HeLa cells by means of gene apoA-I-containing DNA and after recombinant retrovirus apoA-I gene transfer into rat fibroblasts RAT-I, full-value gene expression took place in these cells. The expression was accompanied by the formation of an immunospecific protein product. In addition, human apoA-I gene was transferred into rat liver asa DNA complex with ***conjugate*** :poly(L-Lys) cntdot desialylated orosomucoid. Human apoA-I was found in rat blood serum by enzyme immunoassay 24 hours after i.v. injection of the complex. It was also found that partial hepatectomy performed 30 minutes after the injection of DNA that contained bacterial marker gene lacZ facilitated longer (more than 7 weeks) expression of the marker gene in rat liver. Prospects for using the methods of gene apoA-I transfer for long-term and effective expression of this gene in the liver of mammals were discussed.

L9 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 7
ACCESSION NUMBER: 1997:514717 CAPLUS
DOCUMENT NUMBER: 127:230065
TITLE: Expression of the human apolipoprotein A-I gene transferred into mammalian cells in vitro and rat liver in vivo
AUTHOR(S): Perevozchikov, A. P.; Dizhe, E. B.; Serov, S. M.; Kuryshev, V. Yu.; Arredouani, M.; Parfenova, N. S.; Shavlovskii, M. M.; Nasonkin, I. O.; Drapchinskaya, N. L.; Bondarev, I. E.; Tsarapkina, E. V.; Sukonina, V. E.; Denisenko, A. D.; Gaitshkoki, V. S.; Klimov, A. N.
CORPORATE SOURCE: Institute of Experimental Medicine, Russian Academy of Medical Sciences, St. Petersburg, 197376, Russia
SOURCE: Molecular Biology (Translation of Molekulyarnaya Biologiya (Moscow)) (1997), 31(2), 178-183
CODEN: MOLBBJ; ISSN: 0026-8933
PUBLISHER: Consultants Bureau
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human ***apolipoprotein*** ***A*** - ***I*** gene (apoA-I) under the control of a potent tissue-nonspecific promoter from the cytomegalovirus early gene or the mouse ribosomal protein L32 gene was transferred into cultured mammalian cells. HeLa cells and rat fibroblasts RAT-1 were transfected with apoA-I-contg. DNA using the calcium phosphate technique and recombinant retroviruses, resp. In both cell cultures, the gene was efficiently expressed in an immunospecific protein product. A complex of apoA-I with a ***conjugate*** of poly(L-Lys) and asialic orosomucoid (ASOR) was used to transfect rat liver cells in vivo. Human ***apolipoprotein*** ***A*** - ***I*** (Apo A-I) was detected in rat serum by ELISA 24 h after i.v. injection of the complex. Partial hepatectomy performed 30 min after injecting DNA contg. the lacZ bacterial marker gene promoted its stable (for more than 7 wk) expression in rat liver. Possibilities of using the above methods of gene transfer for efficient stable apoA-I expression in mammalian liver are discussed.

L9 ANSWER 27 OF 38 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 95197550 MEDLINE
DOCUMENT NUMBER: 95197550 PubMed ID: 7890663
TITLE: Carboxyl-terminal domain truncation alters apolipoprotein A-I in vivo catabolism.
AUTHOR: Schmidt H H; Remaley A T; Stonik J A; Ronan R; Wellmann A; Thomas F; Zech L A; Brewer H B Jr; Hoeg J M
CORPORATE SOURCE: Molecular Disease Branch, NHLBI, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Mar 10) 270 (10) 5469-75.

Journal code: [redacted]85121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950427
Last Updated on STN: 19970203
Entered Medline: 19950414

AB ***Apolipoprotein*** ***A*** - ***I*** (apoA-I), the major protein of high density lipoproteins, facilitates reverse cholesterol transport from peripheral tissue to liver. To determine the structural motifs important for modulating the in vivo catabolism of human apoA-I (h-apoA-I), we generated carboxyl-terminal truncation mutants at residues 201 (apoA-I201), 217 (apoA-I217), and 226 (apoA-I226) by site-directed mutagenesis. ApoA-I was expressed in Escherichia coli as a ***fusion*** ***protein*** with the maltose binding protein, which was removed by factor Xa cleavage. The in vivo kinetic analysis of the radioiodinated apoA-I in normolipemic rabbits revealed a markedly increased rate of catabolism for the truncated forms of apoA-I. The fractional catabolic rates (FCR) of 9.10 +/- 1.28/day (+/- S.D.) for apoA-I201, 6.34 +/- 0.81/day for apoA-I217, and 4.42 +/- 0.51/day for apoA-I226 were much faster than the FCR of recombinant intact apoA-I (r-apoA-I, 0.93 +/- 0.07/day) and h-apoA-I (0.91 +/- 0.34/day). All the truncated forms of apoA-I were associated with very high density lipoproteins, whereas the intact recombinant apoA-I (r-apoA-I) and h-apoA-I associated with HDL2 and HDL3. Gel filtration chromatography revealed that in contrast to r-apoA-I, the mutant apoA-I201 associated with a phospholipid-rich rabbit apoA-I containing particle. Analysis by agarose gel electrophoresis demonstrated that the same mutant migrated in the pre-beta position, but not within the alpha position as did r-apoA-I. These results indicate that the carboxyl-terminal region (residue 227-243) of apoA-I is critical in modulating the association of apoA-I with lipoproteins and in vivo metabolism of apoA-I.

L9 ANSWER 28 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 95:437776 SCISEARCH
THE GENUINE ARTICLE: RE377
TITLE: ANTIVIRALS THAT TARGET THE AMINO-TERMINAL DOMAIN OF HIV TYPE-1 GLYCOPROTEIN-41
AUTHOR: GORDON L M (Reprint); WARING A J; CURTAIN C C; KIRKPATRICK A; LEUNG C; FAULL K; MOBLEY P W
CORPORATE SOURCE: UNIV CALIF LOS ANGELES, KING DREW MED CTR, DEPT PEDIAT, MAIL POINT 9, 12021 S WILMINGTON AVE, LOS ANGELES, CA, 90059 (Reprint); MONASH UNIV, DEPT PHYS, CLAYTON, VIC 3052, AUSTRALIA; CSIRO, DIV BIOMOLEC ENGN, PARKVILLE, VIC 3052, AUSTRALIA; UNIV CALIF LOS ANGELES, CTR MOLEC & MED SCI MASS SPECTROMETRY, DEPT CHEM & BIOCHEM, LOS ANGELES, CA, 90024; UNIV CALIF LOS ANGELES, CTR MOLEC & MED SCI MASS SPECTROMETRY, DEPT PSYCHIAT & BIOBEHAV SCI, LOS ANGELES, CA, 90024; CALIF STATE POLYTECH UNIV POMONA, DEPT CHEM, POMONA, CA, 91768
COUNTRY OF AUTHOR: USA; AUSTRALIA
SOURCE: AIDS RESEARCH AND HUMAN RETROVIRUSES, (JUN 1995) Vol. 11, No. 6, pp. 677-686.
ISSN: 0889-2229.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 47

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Functional and structural studies were made to assess whether a class of antiviral agents targets the N-terminal domain of the glycoprotein 41,000 (gp41) of human immunodeficiency virus type 1 (HIV-1), Previous experiments have shown that the amino-terminal peptide (FP-I; 23 amino acids, residues 519-541) of HIV-1 gp41 is cytolytic to both human erythrocytes (non-CD4(+) cells) and Hut-78 cells (CD4(+) lymphocytes), Accordingly, FP-I-induced hemolysis may be used as a surrogate assay for evaluating the role of the N-terminal gp41 domain in HIV-cell interactions, Here, we studied the blocking of FP-I-induced lysis of erythrocytes by the following anti-HIV agents: (1) IgG [i.e.; anti-(518-541) IgG] raised to an immunoconjugate of Arg-FP-I, (2) apolipoprotein A-1 (ape A-1) and a peptide based on apo A-1, (3) dextran sulfate, (4) gp41 peptide (residues 637-666), and (5) anionic human serum albumins, Dose-response curves indicated that their relative potency in inhibiting FP-I-induced hemolysis was approximately correlated with their previously reported anti-HIV activity, Electron spin resonance (ESR)

studies showed that FP-I spin labeled at the N-terminal alanine binds to anti-(518-541) IgG, dextran sulfate, and anionic albumins, The high in vitro antiviral activity and low cytotoxicity of these agents suggest that blocking membrane-FP-I interactions offers a novel approach for AIDS therapy or prophylaxis.

L9 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:467299 CAPLUS
DOCUMENT NUMBER: 119:67299
TITLE: Lipoprotein assays using antibodies to a pan native epitope and recombinant antigens
INVENTOR(S): Smith, Richard S.; Curtiss, Linda K.; Koduri, Kanaka Raju; Witztum, Joseph L.; Young, Stephen G.
PATENT ASSIGNEE(S): Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9307165	A1	19930415	WO 1992-US8634	19921009
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
US 5408038	A	19950418	US 1992-959946	19921008
PRIORITY APPLN. INFO.:			US 1991-774633	19911009
			US 1992-901706	19920628
			US 1992-959946	19921008

AB Methods and compns. are described for detg. LDL in plasma. Native apolipoprotein B-100 (apo B-100) present in LDL particles is immunol. mimicked by a polypeptide of the invention. The polypeptide includes an amino acid sequence corresponding to a pan epitope region of the target apoprotein. A preferred polypeptide is a fusion protein that simultaneously mimics native apo B-100 and native apo A-I. Improved assay systems and methods for detg. HDL and LDL levels in a body fluid sample are also described. Fragment sequences from apo B-100 and apo A-I are included. The monoclonal antibody (MAb) MB47 epitope of apo B-100 was mapped using apo B-100 fragment fusion proteins with .beta.-galactosidase; cloning of apo B-100 fragment cDNA is described. Also described is the prepn. of apo A-I/B-100 fusion proteins as further fusions with a .beta.-galactosidase fragment. In an ELISA, Apo A-I/B-100 fusion protein showed reactivity with both MAb MB47 and anti-apo AI MAb AI-11; the fusion protein did not need to be solubilized (e.g. with a denaturing concn. of SDS) for use in the assay.

L9 ANSWER 30 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 93:726110 SCISEARCH
THE GENUINE ARTICLE: MK130
TITLE: THE AMINO-TERMINAL PEPTIDE OF HIV-1 GP41 INTERACTS WITH HUMAN SERUM-ALBUMIN
AUTHOR: GORDON L M (Reprint); CURTAIN C C; MCCLOYN V; KIRKPATRICK A; MOBLEY P W; WARING A J
CORPORATE SOURCE: UCLA, DREW UNIV KING MED CTR, DEPT PEDIAT, MAIL POINT 9, 12021 WILMINGTON AVE, LOS ANGELES, CA, 90059 (Reprint); MONASH UNIV, DEPT PHYS, CLAYTON, VIC 3168, AUSTRALIA; CALIF STATE UNIV DOMINGUEZ HILLS, DEPT BIOL, CARSON, CA, 90747; CSIRO, DIV BIOMOLEC ENGN, PARKVILLE, VIC 3052, AUSTRALIA; CALIF STATE POLYTECH UNIV POMONA, DEPT CHEM, POMONA, CA, 91768
COUNTRY OF AUTHOR: USA; AUSTRALIA
SOURCE: AIDS RESEARCH AND HUMAN RETROVIRUSES, (NOV 1993) Vol. 9, No. 11, pp. 1145-1156.
ISSN: 0889-2229.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Structural and functional studies were made to assess interactions between human serum albumin (HSA) and the amino-terminal peptide (FP-I; 23-residue peptide 519-541) of glycoprotein 41,000 (gp41) of human immunodeficiency virus type-1 (HIV-1). Circular dichroism (CD) spectroscopy indicated that the peptide binds to albumin with dominant alpha-helical character. Peptide binding to albumin was also examined using FP-I spin labeled at either the amino-terminal alanine (FP-II;

residue 519) or methionine (FP-III; position 537). Electron spin resonance (ESR) spectra of FP-II bound to HSA at 38 degrees C indicated that the spin label at the amino-terminal residue (Ala-519) was motionally restricted. The ESR spectrum of 12-nitroxide stearate (12-NS)-labeled HSA was identical to that obtained with FP-II, indicating that the reporter groups for the 12-NS and FP-II probes are similarly bound to albumin. Contrarily, ESR spectra of HSA labeled with FP-III indicated high mobility for the reporter group (Met-537) at the aqueous-protein interface. This suggests that the N-terminal gp41 peptide binds as an alpha helix (residues 519-536) to fatty acid sites on HSA, such that Ala-519 of the peptide resides in the interior of the protein while Met-537 lies outside the protein in aqueous solution. It is also of interest that addition of HSA to human red blood cells dramatically reduced the ability of FP-I to induce hemolysis, presumably through peptide-albumin binding that inhibited FP-I interactions with red cell membranes. The significance of these results focuses on the following three points. The first is that high serum levels of albumin may limit the efficacy of anti-HIV therapies using peptides based on the N-terminal gp41 domain. The second is that the elucidation of FIP-I and HSA interactions with physical techniques may provide clues on the molecular features underlying viral FP-I combination with receptors on the target cell surface. Last, the affinity of albumin for the N-terminal gp41 peptide may play a subordinate role in the blocking of HIV infectivity in vitro that has been reported for chemically modified albumins.

L9 ANSWER 31 OF 38 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 93:89289 SCISEARCH
THE GENUINE ARTICLE: KL312
TITLE: PRODUCTION OF AUTHENTIC HUMAN PROAPOLIPOPROTEIN-A-I IN ESCHERICHIA-COLI - STRATEGIES FOR THE REMOVAL OF THE AMINO-TERMINAL METHIONINE
AUTHOR: MOGUILEVSKY N; VARSALONA F; GUILLAUME J P; GILLES P; BOLLEN A (Reprint); ROOBOL K
CORPORATE SOURCE: UNIV BRUSSELS, 24 RUE IND, B-1400 NIVELLES, BELGIUM; UCB BIOPROD, B-1420 BRAINE LALLEUD, BELGIUM; UCB PHARMA, B-1420 BRAINE LALLEUD, BELGIUM
COUNTRY OF AUTHOR: BELGIUM
SOURCE: JOURNAL OF BIOTECHNOLOGY, (JAN 1993) Vol. 27, No. 2, pp. 159-172.
ISSN: 0168-1656.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: AGRI
LANGUAGE: ENGLISH
REFERENCE COUNT: 37
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Several methods were compared with respect to the production of authentic, N-terminal methionine-free proapolipoprotein A-I in engineered Escherichia coli bacteria. A first approach consisted of treating the purified methionylated recombinant protein with an amino-peptidase, purified from Aeromonas proteolytica. A second series of strategies was based on the construction of proapo A-I encoding cassettes carrying built-in recognition sites suitable for specific in vitro cleavage of the products with kallikrein and enterokinase, respectively. Along the same line, a fusion between ubiquitin and proapo A-I was produced in E. coli with the prospect to achieve post-purification cleavage with yeast ubiquitin hydrolase. Finally, proapo A-I was fused to the signal peptide of the bacterial outer membrane protein, OmpA, aiming at an in situ conversion to authentic proapo A-I during secretion to the bacterial periplasm.

The data showed that, out of these five systems, the OmpA signal peptide system and, to a lesser extent, the one involving the fusion to ubiquitin were the most efficient in yielding authentic proapo A-I from engineered Escherichia coli.

L9 ANSWER 32 OF 38 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 93047287 MEDLINE
DOCUMENT NUMBER: 93047287 PubMed ID: 1424123
TITLE: Pre-beta high-density lipoprotein determined by immunoblotting with chemiluminescent detection.
AUTHOR: O'Kane M J; Wisdom G B; McEneny J; McFerran N V; Trimble E R
CORPORATE SOURCE: Department of Clinical Biochemistry, Royal Victoria Hospital, Belfast, UK.
SOURCE: CLINICAL CHEMISTRY, (1992 Nov) 38 (11) 2273-7.
Journal code: 9421549. ISSN: 0009-9147.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Jou s
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921223

AB We describe a novel assay of pre-beta high-density lipoprotein (HDL), a unique ***apolipoprotein*** ***A*** - ***I*** (apo A-I)-containing lipoprotein particle. The pre-beta and alpha lipoproteins are separated by electrophoresis in agarose and transferred onto a membrane by capillary blotting. The membrane blot is sequentially incubated with sheep anti-human apo A-I antiserum and then with a ***conjugate*** of rabbit anti-sheep immunoglobulin and horseradish peroxidase. Chemiluminescence formed by the peroxidase-catalyzed oxidation of luminol in the presence of an enhancer is captured on photographic film, and the pre-beta HDL band is quantified by transmission densitometry. The assay is calibrated with standards prepared from a reference serum diluted in 9 mol/L urea. Within-batch precision (CV) at pre-beta HDL concentrations of 22.1 and 44.3 mg/L was 7% and 4.9% respectively. Pre-beta HDL contained 1.6% (0.65-2.6%, mean and range) of total serum apo A-I in 30 normolipidemic subjects.

L9 ANSWER 33 OF 38 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 93003772 MEDLINE
DOCUMENT NUMBER: 93003772 PubMed ID: 1391226
TITLE: [Thyroid hormone conjugates with rhodamine B as fluorescent ligands of human plasma transport proteins].
Kon''iugaty tireoidnykh gormonov s rodaminom B kak fluorestsentnye ligandy transportnykh belkov plazmy krovi cheloveka.
AUTHOR: Ermolenko M N; Fil'chenkov N A; Sviridov O V
SOURCE: BIOKHIMIIA, (1992 Aug) 57 (8) 1271-7.
Journal code: 0372667. ISSN: 0320-9725.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921125

AB ***Conjugates*** of thyroxine (T4) and triiodothyronine (T3) with rhodamine B in which the hormone and the fluorescent dye are linked via a thiourea bond have been synthesized. These ***conjugates*** possess an ability to inhibit in a competitive manner the binding of [125I]T4 to three protein preparations: T4-binding globulin (TBG), ***apolipoprotein*** ***A*** - ***I*** (ApoA-I), and high density lipoprotein particles (ApoA-I-HDL) isolated from human serum by T4-Sepharose 4B chromatography and further purified. The following values of association constants have been estimated: for the T4 derivative-3 x 10(7) M-1 (TBG), 4.1 x 10(5) M-1 (ApoA-I), and 4.2 x 10(5) M-1 (ApoA-I-HDL); for the T3 derivative-1.6 x 10(7) M-1 (TBG), 5.3 x 10(5) M-1 (ApoA-I), and 5.4 x 10(5) M-1 (ApoA-I-HDL). The binding of rhodamine B-labeled thyroid hormones to TBG or ApoA-I do not alter significantly the parameters of rhodamine B chromophore absorption and fluorescence. The interaction of the ***conjugates*** with ApoI-HDL leads to a significant enhancement of the absorption intensity and a 3 nm blue shift in the absorption maximum as well as to a 1.5-fold increase in the fluorescence band amplitude at 586 nm. Biological and fluorescent properties of T4 and T3 derivatives suggest that these compounds may be a useful tool in fluorescence studies of plasma binding protein-driven transport of thyroid hormones in model biological systems.

L9 ANSWER 34 OF 38 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 92353111 MEDLINE
DOCUMENT NUMBER: 92353111 PubMed ID: 1643096
TITLE: Concentration and distribution of apolipoproteins A-I and E in normolipidemic, WHHL and diet-induced hyperlipidemic rabbit sera.
AUTHOR: Mezdour H; Nomura S; Yamamura T; Yamamoto A
CORPORATE SOURCE: National Cardiovascular Center Research Institute, Department of Etiology and Pathophysiology, Osaka, Japan.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1992 Jul 29) 1127 (2) 116-23.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Jou[redacted]s
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19920925
Last Updated on STN: 19920925
Entered Medline: 19920904

AB Two sandwich-type enzyme immunoassays have been developed to measure ***apolipoproteins*** ***A*** - ***I*** and E in rabbit serum. Specific goat antibodies were purified by affinity chromatography and used both for coating and for preparing antibody-peroxydase ***conjugates*** . The sensitivity of these assays is sufficient to allow studies of apo A-I and E distribution in lipoproteins fractionated by gel filtration from 50 microliters of serum. In WHHL rabbits, apo A-I is 5-fold lower (5.2 +/- 2.5 mg/dl) and apo E is 8-fold higher (9.9 +/- 3.5 mg/dl) than in normolipidemic rabbits (29 +/- 4.3 mg/dl and 1.3 +/- 0.5 mg/dl, respectively). In hyperlipidemic rabbits, fed 2 months on a 0.5% cholesterol diet, the apo A-I level was similar (32 +/- 12 mg/dl) to that of normolipidemic rabbits, but the apo E level is 12-fold higher (15.1 +/- 5.5 mg/dl). In addition, HDL particles were enriched with cholesterol and apo E. The bulk of apo E and cholesterol is located in large beta-VLDL in diet-induced hyperlipidemia, whereas they are mainly located in smaller size beta-VLDL in WHHL rabbits. In normolipidemic rabbits apo E occurs mainly in HDL, and cholesterol is distributed in the main three lipoprotein fractions VLDL, LDL and HDL. Interestingly, HDL of WHHL rabbit are deficient in apo A-I. These results are compatible with profound perturbations of lipoprotein composition and metabolism in atherogenic hyperlipidemia.

L9 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:570648 CAPLUS
DOCUMENT NUMBER: 111:170648
TITLE: Method and kit for the competitive immunoassay of apolipoproteins using immobilized antibody and antigenic hybrid label protein
INVENTOR(S): Baralle, Francisco Ernesto; Sidoli, Alessandro
PATENT ASSIGNEE(S): Istituto Sieroterapico Milanese S. Belfanti, Italy
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 301667	A1	19890201	EP 1988-201622	19880727
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
WO 8901164	A1	19890209	WO 1988-GB616	19880728
W: JP, US				
GB 2208317	A1	19890322	GB 1988-18031	19880728
JP 02500164	T2	19900125	JP 1988-506237	19880728
PRIORITY APPLN. INFO.:			GB 1987-17791	19870728
			WO 1988-GB616	19880728

AB Apolipoprotein is detected or estd. in a sample by (a) contacting the sample with a solid support having immobilized antibody to apolipoprotein and with a fused protein comprising an antigenic part of the apolipoprotein and a label protein; and (b) observing or measuring the label protein either bound or not bound to the support. A test hit comprises the immobilized antibody and the hybrid protein. The assay is called RIECA (Recombinant immuno Enzymic Competition Assay). ***Apolipoproteins*** ***A*** - ***I*** and B was detd. in whole blood, serum, and plasma using specific monoclonal antibodies immobilized in 96-well plates and .beta.-galactosidase ***fusion*** ***proteins*** [prepd. by expression of Escherichia coli plasmid pISMAI (coding for the enzyme and for apo-A-I) or plasmid pISMBI (coding for the enzyme and coding sequences of apolipoprotein B-1).

L9 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:135501 CAPLUS
DOCUMENT NUMBER: 112:135501
TITLE: Characterization of anti-apolipoprotein A-I monoclonal antibodies and their use in the measurement of apolipoprotein A-I by a two-site enzyme immunoassay
AUTHOR(S): Dubois, D. Y.; Malmendier, C. L.
CORPORATE SOURCE: Res. Found. Atherosclerosis, Brussels, Belg.
SOURCE: Journal of Immunological Methods (1989), 125(1-2), 215-23

CODEN: JIMMBG; ISSN: 0022-1759
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Six monoclonal antibodies raised against pure ***apolipoprotein*** ***A*** - ***I*** (apo A-I) or high-d. lipoprotein (HDL) were characterized for epitope specificity by enzyme immunoassays and RIAs, immunodiffusion, and affinity chromatog. The 6 antibodies were classified into 3 groups according to the region of apo A-I they reacted with. The antibody VI10H, from group II, appeared to recognize a region fully exposed on native HDL-apo A-I, whereas group I comprised antibodies specific for a partially masked region. Group III comprised only 1 antibody. Use of the nonionic detergent Tween 20 in the immunoassays permitted antibodies from the 3 groups to react with their resp. epitope on native HDL-apo A-I. An antibody from group I (V4F) was chosen as the first antibody and VI10H, the antibody showing the highest affinity, was chosen for the anti-A-I-peroxidase ***conjugate*** in a 2-site enzyme immunoassay.

L9 ANSWER 37 OF 38 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 88077095 MEDLINE
DOCUMENT NUMBER: 88077095 PubMed ID: 3120726
TITLE: Human proapolipoprotein A-I: development of an antibody to the propeptide as a probe of apolipoprotein A-I biosynthesis and processing.
AUTHOR: Hospattankar A V; Fairwell T; Appella E; Meng M; Brewer H B Jr
CORPORATE SOURCE: Molecular Disease Branch, National Heart, Lung and Blood Institute, Bethesda, Maryland 20892.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1987 Nov 30) 149 (1) 289-96.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198801
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19880112
AB In human plasma, ***apolipoprotein*** ***A*** - ***I*** is present as pro and mature isoproteins. The development of a highly specific antibody to the pro isoprotein of apoA-I has been difficult due to the close structural similarity between the pro and mature isoforms of apoA-I. To sermount this difficulty, a peptide was synthesized by the solid phase method which corresponded to the amino acid sequence present in the pro region of apoA-I. The synthetic peptide was coupled to serum albumin and the ***conjugate*** utilized to immunize rabbits for antibody production. Immunoblot analysis of purified proapoA-I and mature apoA-I revealed that the antibody was specific for the propeptide of apoA-I. Analysis of apoA-I in the plasma from a Tangier disease patient and newly secreted apoA-I from HepG2 cells clearly demonstrated the isoforms which contained the proisoprotein. The proapoA-I specific antibody should prove to be a useful tool in developing a radioimmunoassay for quantitation of the proisoprotein in plasma, isolation of proapoA-I from normal and dyslipoproteinemic subjects by immunoaffinity chromatography and in studies related to the synthesis and processing of apoA-I.

L9 ANSWER 38 OF 38 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 83215150 MEDLINE
DOCUMENT NUMBER: 83215150 PubMed ID: 6406642
TITLE: Competitive enzyme immunoassay for apolipoprotein A-II.
AUTHOR: Dufaux B; Ilsemann K; Assmann G
SOURCE: JOURNAL OF CLINICAL CHEMISTRY AND CLINICAL BIOCHEMISTRY, (1983 Jan) 21 (1) 39-43.
Journal code: 7701860. ISSN: 0340-076X.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198307
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19830708
AB A competitive enzyme immunoassay for apolipoprotein A-II was developed. Microtitre plates were used as a solid phase and coated with anti-apolipoprotein A-II antibodies. Purified apolipoprotein A-II,

labelled with horseradish peroxidase was used as competing ligand. The assay was examined with respect to the optimal amounts of specific anti-apolipoprotein A-II antibodies and apolipoprotein A-II-enzyme ***conjugate*** . The displacement curves showed a good parallelism between serum and purified apolipoprotein A-II. Delipidation of serum did not affect the content of apolipoprotein A-II. Cross-reactivity with ***apolipoprotein*** ***A*** - ***I*** was minimal. The intra- and inter-assay coefficients of variation in the medium range were 9.0 and 11.8% respectively. The assay might be well-suited for clinical routine.

=> d his

(FILE 'HOME' ENTERED AT 18:35:30 ON 08 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 18:35:47 ON 08 JUL 2003

```
L1         21207 S APOLIPOPROTEIN A-I
L2        301385 S (FC DOMAIN) OR (POLYETHYLENE GLYCOL) OR PEG OR POLYLYSINE OR
L3            76 S L1 (P) L2
L4             2 S L3 (P) (CONJUGATE OR FUSION)
L5             2 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)
L6            43 S L1 (P) (FUSION PROTEIN)
L7            36 S L1 (P) CONJUGATE
L8            79 S L6 OR L7
L9            38 DUPLICATE REMOVE L8 (41 DUPLICATES REMOVED)
L10        50011 S LINKER
L11            0 S L9 (P) L10
```

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	121.78	121.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.37	-12.37

STN INTERNATIONAL LOGOFF AT 18:43:58 ON 08 JUL 2003

Kam 09/840,669

=> d his 1

(FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 14:23:31 ON 06 MAY 2003)
L25 45 DUP REM L24 (69 DUPLICATES REMOVED)

=> d que 125
L1 3067 SEA KOHNO T?/AU
L2 1 SEA L1 AND AMPHIPATHIC
L3 7031 SEA (APOA1 OR APOAI OR (APO(A)(A1 OR AI)))
L4 12196 SEA (APO(A) A(A)(1 OR I))
L5 125733 SEA APOLIPOPROTEIN#
L6 30019 SEA L5 (A)(A1 OR AI OR A(A) 1 OR A(A) I)
L7 38085 SEA L3 OR L4 OR L6
L8 177 SEA L7 (5A) AMPHIPATH?
L9 79 SEA L8 AND (HYPERCHOLESTER? OR CHOLESTER?)
L10 13 SEA L8 AND (INFECT?(5A)(VIRAL? OR VIRUS?))
L11 286 SEA L7 (5A)(HELIX OR HELIC##)
L12 6 SEA L8 AND IGG?
L21 114 SEA L2 OR L9 OR L10 OR (L12 OR L13 OR L14 OR L15 OR L16 OR L17) OR L19 OR L20
L23 1 SEA (L8 OR L11)(5A)(VEHIC? OR CARRIER?)
L24 114 SEA L21 OR L23
L25 45 DUP REM L24 (69 DUPLICATES REMOVED)

=> d ibib abs l25 1-45

L25 ANSWER 1 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:242031 HCAPLUS
DOCUMENT NUMBER: 138:281126
TITLE: Peptide and peptide analog apolipoprotein A-I agonists, and their use to treat dyslipidemic disorders
INVENTOR(S): Dasseux, Jean-louis; Sekul, Renate; Buttner, Klaus; Cornut, Isabelle; Metz, Gunther
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. 465,718.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003060604	A1	20030327	US 2002-99574	20020315

PRIORITY APPLN. INFO.: US 1999-465718 A1 19991217
AB The invention provides peptides and peptide analogs that mimic the structural and pharmacol. properties of human ApoA-I. The peptides and peptide analogs are useful to treat a variety of disorders assocd. with dyslipidemia.

L25 ANSWER 2 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:174464 HCAPLUS
DOCUMENT NUMBER: 138:226693
TITLE: Class A amphipathic helix-containing peptides as oral active anti-atherosclerotic agents

Search completed by David Schreiber 308-4292

Kam 09/840,669

INVENTOR(S): Fogelman, Alan M.; Anantharamaiah, Gattadahalli M.; Navab, Mohamad
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 645,454.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003045460	A1	20030306	US 2001-896841	20010629

PRIORITY APPLN. INFO.: US 2000-645454 A2 20000824

AB This invention provides novel peptides having class A amphipathic helix that ameliorate one or more symptoms of atherosclerosis. The peptides are highly stable and readily administered via an oral route.

L25 ANSWER 3 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:798252 HCAPLUS
DOCUMENT NUMBER: 135:362518
TITLE: Apo-AI/AII peptide derivatives for hypocholesteremic and antiviral therapy
INVENTOR(S): **Kohno, Tadahiko**
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081376	A2	20011101	WO 2001-US13068	20010423
WO 2001081376	A3	20030109		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003040470	A1	20030227	US 2001-840669	20010423
EP 1290013	A2	20030312	EP 2001-930664	20010423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-198920P P 20000421
WO 2001-US13068 W 20010423

AB The present invention concerns therapeutic agents that mimic the activity of **Apo-AI amphipathic helix** peptide. In accordance with the present invention, the compds. of the invention comprise: (a) a **Apo-AI amphipathic helix** peptide or **Apo-AI amphipathic helix** peptide-**mimetic** domain, preferably the amino acid sequence of SEQ ID NO:7, or sequences derived therefrom by phage display,

Search completed by David Schreiber 308-4292

RNA-peptide screening, or the other techniques mentioned above; and (b) a vehicle, such as a polymer (e.g., PEG or dextran) or an **Fc** domain, which is preferred; wherein the vehicle, preferably an **Fc** domain, is covalently attached to the **Apo-AI amphipathic helix** peptide or **Apo-AI amphipathic helix** peptide-**mimetic** domain. The **vehicle** and the **Apo-AI amphipathic helix** peptide or **Apo-AI amphipathic helix** peptide-**mimetic** domain may be linked through the N- or C-terminus of the **Apo-AI amphipathic helix** peptide or **Apo-AI amphipathic helix** peptide-**mimetic** domain, as described further below. The preferred vehicle is an **Fc** domain, and the preferred **Fc** domain is an **IgG Fc** domain. Preferred **Apo-AI amphipathic helix** peptide or **Apo-AI amphipathic helix** peptide-**mimetic** domains comprise the amino acid sequences described in Table 1. Other **Apo-AI amphipathic helix** peptide or **Apo-AI amphipathic helix** peptide-**mimetic** domains can be generated by phage display, RNA-peptide screening and the other techniques mentioned herein.

L25 ANSWER 4 OF 45 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002003429 MEDLINE
DOCUMENT NUMBER: 21623605 PubMed ID: 11602583
TITLE: The N-terminal globular domain and the first class A **amphipathic** helix of **apolipoprotein A-I** are important for lecithin: **cholesterol** acyltransferase activation and the maturation of high density lipoprotein in vivo.
AUTHOR: Scott B R; McManus D C; Franklin V; McKenzie A G; Neville T; Sparks D L; Marcel Y L
CORPORATE SOURCE: Lipoprotein and Atherosclerosis Research Group, University of Ottawa Heart Institute, Ottawa, Ontario K1Y 4W7, Canada.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Dec 28) 276 (52) 48716-24.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020102
Last Updated on STN: 20030105
Entered Medline: 20020131

AB To investigate the role of the N terminus of apolipoprotein A-I (apoA-I) in the maturation of high density lipoproteins (HDL), two N-terminal mutants with deletions of residues 1-43 and 1-65 (referred to as Delta 1-43 and Delta 1-65 apoA-I) were studied. In vitro, these deletions had little effect on cellular **cholesterol** efflux from macrophages but LCAT activation was reduced by 50 and 70% for the Delta 1-43 and Delta 1-65 apoA-I mutants, respectively, relative to wild-type (Wt) apoA-I. To further define the role of the N terminus of apoA-I in HDL maturation, we constructed recombinant adenoviruses containing Wt apoA-I and two similar mutants with deletions of residues 7-43 and 7-65 (referred to as Delta 7-43 and Delta 7-65 apoA-I, respectively). Residues 1-6 were not removed in these mutants to allow proper cleavage of the pro-sequence in vivo. Following injection of these adenoviruses into apoA-I-deficient mice, plasma concentrations of both Delta 7-43 and Delta 7-65 apoA-I were

reduced 4-fold relative to Wt apoA-I. The N-terminal deletion mutants, in particular Delta 7-65 apoA-I, were associated with greater proportions of pre beta-HDL and accumulated fewer HDL **cholesteryl** esters relative to Wt apoA-I. Wt and Delta 7-43 apoA-I formed predominantly alpha-migrating and spherical HDL, whereas Delta 7-65 apoA-I formed only pre beta-HDL of discoidal morphology. This demonstrates that deletion of the first class A amphipathic alpha-helix has a profound additive effect in vivo over the deletion of the globular domain alone (amino acids 1-43) indicating its important role in the production of mature alpha-migrating HDL. In summary, the combined in vitro and in vivo studies demonstrate a role for the N terminus of apoA-I in lecithin:**cholesterol** acyltransferase activation and the requirement of the first class A amphipathic alpha-helix for the maturation of HDL in vivo.

L25 ANSWER 5 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2002:38102 SCISEARCH
THE GENUINE ARTICLE: 505ZP
TITLE: C-13 NMR method for the determination of peptide and protein binding sites in lipid bilayers and emulsions
AUTHOR: Okamura E (Reprint); Kimura T; Nakahara M; Tanaka M; Handa T; Saito H
CORPORATE SOURCE: Kyoto Univ, Inst Chem Res, Kyoto 6110011, Japan (Reprint); Kyoto Univ, Grad Sch Pharmaceut Sci, Sakyo Ku, Kyoto 6068501, Japan; Natl Inst Hlth Sci, Osaka Branch, Osaka 5400006, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: JOURNAL OF PHYSICAL CHEMISTRY B, (20 DEC 2001) Vol. 105, No. 50, pp. 12616-12621.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 1089-5647.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 31

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The natural abundance C-13 NMR method was applied to directly determine the binding site of peptides and proteins in lipid bilayers and emulsions on the atomic level. Reliable NMR criteria for the location and depth of peptides and proteins in membranes were shown by the chemical shift and line width analyses, which reproduced not only the deep penetration of a transmembrane channel peptide gramicidin A but also the superficial binding of Ac-18A-NH2 (Ac-DWLKAFYDKVAEKLKEAF-NH2), a synthetic model peptide of **amphipathic** helices of plasma **apolipoprotein A-I** (apoA-I). The reliability was ensured by the NMR information, which was consistent with the recent X-ray diffraction study of Ac-18A-NH2 in oriented lipid bilayers (Hristova et al. J. Mol. Biol. 1999, 290, 99). Our method first provided the atomic-level evidence for native apoA-I binding in egg phosphatidylcholine (EPC) vesicles and triolein (TO)-EPC emulsions as spherical model lipoproteins. Membrane perturbation was most significant at EPC glycerol and ester carbonyl sites when apoA-I was bound to EPC small unilamellar vesicles. This indicates not deep but shallow penetration of apoA-I into the membrane interface whose polarity is intermediate between water and the hydrophobic core. The binding preference for the interfacial site of membranes was confirmed by the common binding site between apoA-I and its model peptide Ac-18A-NH2. Membrane structural modulation by apoA-I was, however, moderate at the bilayer headgroup and the alkyl chain region near the interface. The shallow penetration of apoA-I was also found in TO-EPC emulsions, a protein-free model of triglyceride-rich lipoproteins (chylomicrons) in

plasma.

L25 ANSWER 6 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:310178 HCAPLUS
DOCUMENT NUMBER: 135:102279
TITLE: A new synthetic class A amphipathic peptide analogue protects mice from diet-induced atherosclerosis
AUTHOR(S): Garber, David W.; Datta, Geeta; Chaddha, Manjula; Palgunachari, M. N.; Hama, Susan Y.; Navab, Mohamad; Fogelman, Alan M.; Segrest, Jere P.; Anantharamaiah, G. M.
CORPORATE SOURCE: The Atherosclerosis Research Unit and the Departments of Medicine and Biochemistry and Molecular Genetics, The University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SOURCE: Journal of Lipid Research (2001), 42(4), 545-552
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several synthetic class A peptide analogs have been shown to mimic many of the properties of human apo A-I in vitro. A new peptide [acetyl-(AspTrpLeuLysAlaPheTyrAspLysValPheGluLysPheLysGluPhePhe)-NH2; 5F], with increased amphipathicity, was administered by i.p. injection, 20 .mu.g/day for 16 wk, to C57BL/6J mice fed an atherogenic diet. Mouse apo A-I (MoA-I) (50 .mu.g/day) or phosphate-buffered saline (PBS) injections were given to other mice as controls. Total plasma **cholesterol** levels and lipoprotein profiles were not significantly different between the treated and control groups, except that the mice receiving 5F or MoA-I had lower high d. lipoprotein (HDL) **cholesterol** when calcd. as a percentage of total **cholesterol**. No toxicity or prodn. of antibodies to the injected materials was obsd. When HDL was isolated from high fat diet-administered mice injected with 5F and presented to human artery wall cells in vitro together with human low d. lipoprotein (LDL), there were substantially fewer lipid hydroperoxides formed and substantially less LDL-induced monocyte chemotactic activity than with HDL from PBS-injected animals. Injection of human apo A-I produced effects similar to 5F on lipid peroxide formation and LDL-induced monocyte chemotactic activity, but injection of MoA-I was significantly less effective in reducing lipid hydroperoxide formation or lowering LDL-induced monocyte chemotactic activity. Mice receiving peptide 5F had significantly less aortic atherosclerotic lesion area compared with mice receiving PBS, whereas lesion area in mice receiving MoA-I was similar to that of the PBS-injected animals. This is the first in vivo demonstration that a model class A amphipathic helical peptide has antiatherosclerotic properties. We conclude that 5F inhibits lesion formation in high fat diet-administered mice by a mechanism that does not involve changes in the lipoprotein profile, and may have potential in the prevention and treatment of atherosclerosis.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 45 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001325773 MEDLINE
DOCUMENT NUMBER: 21225023 PubMed ID: 11325616
TITLE: Functional similarities of human and chicken apolipoprotein A-I: dependence on secondary and tertiary rather than primary structure.
AUTHOR: Kiss R S; Ryan R O; Francis G A

Search completed by David Schreiber 308-4292

CORPORATE SOURCE: Department of Biochemistry, University of Alberta, Edmonton, Canada.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (2001 Apr 30) 1531 (3) 251-9.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010611
Last Updated on STN: 20010611
Entered Medline: 20010607

AB To investigate the sequence requirements for apolipoprotein (apo) AI functions, comparisons of human and chicken apoAI were performed. In lipid binding assays, chicken apoAI was capable of transforming phospholipid vesicles into discoidal bilayer structures, similar in both size and apolipoprotein content to those produced with human apoAI under the same conditions. Human and chicken apoAI were indistinguishable in their relative abilities to prevent phospholipase C-induced aggregation of human low density lipoprotein. This activity, which is dependent upon formation of a stable interaction with the modified lipoprotein, represents a sensitive measure of apolipoprotein association with spherical lipoprotein particles. The ability of chicken versus human apoAI to mobilize the regulatory pool of **cholesterol** available for esterification by acyl-CoA:**cholesterol** acyltransferase by human fibroblasts was also assessed. Lipid-free chicken and human apoAI were equivalent in their ability to deplete **cholesterol** from this pool, as were intact chicken high density lipoprotein (HDL) and human HDL(3). Based on the overall sequence identity of chicken and human apoAI (48%), and comparison of regions thought to be responsible for key **apoAI** functions, these data indicate that **amphipathic** alpha-helical structure, rather than specific amino acid sequence, is the major determinant of apoAI lipid binding and ability to mobilize the regulatory pool of cellular **cholesterol**.

L25 ANSWER 8 OF 45 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 3

ACCESSION NUMBER: 2001:570694 HCAPLUS
DOCUMENT NUMBER: 135:284581
TITLE: Toward the design of peptide mimics of antiatherogenic apolipoproteins A-I and E
AUTHOR(S): Anantharamaiah, G. M.; Datta, G.; Garber, D. W.
CORPORATE SOURCE: Department of Medicine, Biochemistry and Molecular Genetics, The University of Alabama at Birmingham Medical Center, Birmingham, AL, 35294, USA
SOURCE: Current Science (2001), 81(1), 53-65
CODEN: CUSCAM; ISSN: 0011-3891
PUBLISHER: Current Science Association
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. Two major markers for atherosclerosis are increased plasma **cholesterol** levels and low levels of high d. lipoproteins (HDL). Human apolipoprotein (apo) A-I, the major protein component of HDL, has been shown to inhibit atherosclerosis in vivo without altering plasma **cholesterol** levels, perhaps through its antioxidant effect on low d. lipoproteins (LDL). On the other hand, apo E inhibits atherosclerosis by enhancing the uptake of atherogenic lipoproteins by the liver and thus lowering plasma **cholesterol** levels. The class A amphipathic peptide 18A and its analogs, designed based on the

lipid-assocg. **amphipathic** helical motif present in **apo A-I**, have been shown by us to mimic properties of apo A-I. Recently, we have shown that administration of an analog of 18A was also able to inhibit atherosclerosis in atherosclerosis-sensitive mice, similar to apo A-I, without altering the plasma **cholesterol** levels. Based on the presence of two domains in apo E, the lipid-assocg. domain and the receptor-binding cationic domain, linking residues 141-150 of apo E to 18A resulted in a peptide that enhanced the uptake of atherogenic lipoproteins in vitro. Administration of this peptide into dyslipidemic mice showed a dramatic decrease in plasma **cholesterol** levels. These results demonstrate the potential for the design of peptides to ameliorate atherosclerosis, the no. one cause of mortality in the developed countries.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 45 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 4
ACCESSION NUMBER: 2001118449 EMBASE
TITLE: Structural models of human apolipoprotein A-I: A critical analysis and review.
AUTHOR: Brouillette C.G.; Anantharamaiah G.M.; Engler J.A.; Borhani D.W.
CORPORATE SOURCE: C.G. Brouillette, Ctr. for Biophysical Sciences/Eng., University of Alabama, 1918 University Boulevard, Birmingham, AL 35294-0005, United States. christie@uab.edu
SOURCE: Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids, (30 Mar 2001) 1531/1-2 (4-46).
Refs: 262
ISSN: 1388-1981 CODEN: BBMLFG
PUBLISHER IDENT.: S 1388-1981(01)00081-6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Human apolipoprotein (apo) A-I has been the subject of intense investigation because of its well-documented anti-atherogenic properties. About 70% of the protein found in high density lipoprotein complexes is apo A-I, a molecule that contains a series of highly homologous amphiphatic .alpha.-helices. A number of significant experimental observations have allowed increasing sophisticated structural models for both the lipid-bound and the lipid-free forms of the apo A-I molecule to be tested critically. It seems clear, for example, that interactions between **amphipathic** domains in **apo A-I** may be crucial to understanding the dynamic nature of the molecule and the pathways by which the lipid-free molecule binds to lipid, both in a discoidal and a spherical particle. The state of the art of these structural studies is discussed and placed in context with current models and concepts of the physiological role of apo A-I and high-density lipoprotein in atherosclerosis and lipid metabolism. .COPYRGT. 2001 Elsevier Science B.V.

L25 ANSWER 10 OF 45 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000396465 MEDLINE
DOCUMENT NUMBER: 20317084 PubMed ID: 10858447
TITLE: Binding and cross-linking studies show that scavenger receptor BI interacts with multiple sites in **apolipoprotein A-I** and identify

the class A **amphipathic** alpha-helix as a recognition motif.

AUTHOR: Williams D L; de La Llera-Moya M; Thuahnai S T; Lund-Katz S; Connelly M A; Azhar S; Anantharamaiah G M; Phillips M C

CORPORATE SOURCE: Department of Pharmacological Sciences, University Medical Center, State University of New York, Stony Brook, New York 11794, USA.. dave@pharm.sunysb.edu

CONTRACT NUMBER: DK 49705 (NIDDK)
HL 22633 (NHLBI)
HL 58012 (NHLBI)
+

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Jun 23) 275 (25) 18897-904.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000816

AB Scavenger receptor, class B, type I (SR-BI) mediates the selective uptake of high density lipoprotein (HDL) **cholesteryl** ester without the uptake and degradation of the particle. In transfected cells SR-BI recognizes HDL, low density lipoprotein (LDL) and modified LDL, protein-free lipid vesicles containing anionic phospholipids, and recombinant lipoproteins containing apolipoprotein (apo) A-I, apoA-II, apoE, or apoCIII. The molecular basis for the recognition of such diverse ligands by SR-BI is unknown. We have used direct binding analysis and chemical cross-linking to examine the interaction of murine (m) SR-BI with apoA-I, the major protein of HDL. The results show that apoA-I in apoA-I/palmitoyl-oleoylphosphatidylcholine discs, HDL(3), or in a lipid-free state binds to mSR-BI with high affinity (K(d) congruent with 5-8 microgram/ml). ApoA-I in each of these forms was efficiently cross-linked to cell surface mSR-BI, indicating that direct protein-protein contacts are the predominant feature that drives the interaction between HDL and mSR-BI. When complexed with dimyristoylphosphatidylcholine, the N-terminal and C-terminal CNBr fragments of apoA-I each bound to SR-BI in a saturable, high affinity manner, and each cross-linked efficiently to mSR-BI. Thus, mSR-BI recognizes multiple sites in apoA-I. A model class A amphipathic alpha-helix, 37pA, also showed high affinity binding and cross-linking to mSR-BI. These studies identify the amphipathic alpha-helix as a recognition motif for SR-BI and lead to the hypothesis that mSR-BI interacts with HDL via the amphipathic alpha-helical repeat units of apoA-I. This hypothesis explains the interaction of SR-BI with a wide variety of apolipoproteins via a specific secondary structure, the class A amphipathic alpha-helix, that is a common structural motif in the apolipoproteins of HDL, as well as LDL.

L25 ANSWER 11 OF 45 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 2000138250 MEDLINE
DOCUMENT NUMBER: 20138250 PubMed ID: 10671546

TITLE: Distinct central **amphipathic** alpha-helices in **apolipoprotein A-I** contribute to the in vivo maturation of high density lipoprotein by either activating lecithin-**cholesterol** acyltransferase or binding lipids.

Search completed by David Schreiber 308-4292

Kam 09/840,669

AUTHOR: McManus D C; Scott B R; Frank P G; Franklin V; Schultz J R; Marcel Y L
CORPORATE SOURCE: Lipoprotein and Atherosclerosis Research Group and the Department of Pathology and Laboratory Medicine, University of Ottawa Heart Institute, Ottawa, Ontario K1Y 4W7, Canada.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Feb 18) 275 (7) 5043-51.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000321

AB Recombinant adenoviruses with cDNAs for human apolipoprotein A-I (wild type (wt) apoA-I) and three mutants, referred to as Delta4-5A-I, Delta5-6A-I, and Delta6-7A-I, that have deletions removing regions coding for amino acids 100-143, 122-165, and 144-186, respectively, were created to study structure/function relationships of apoA-I in vivo. All mutants were expressed at lower concentrations than wt apoA-I in plasma of fasting apoA-I-deficient mice. The Delta5-6A-I mutant was found primarily in the lipid-poor high density lipoprotein (HDL) pool and at lower concentrations than Delta4-5A-I and Delta6-7A-I that formed more buoyant HDL(2/3) particles. At an elevated adenovirus dose and earlier blood sampling from fed mice, both Delta5-6A-I and Delta6-7A-I increased HDL-free **cholesterol** and phospholipid but not **cholesteryl** ester. In contrast, wt apoA-I and Delta4-5A-I produced significant increases in HDL **cholesteryl** ester. Further analysis showed that Delta6-7A-I and native apoA-I could bind similar amounts of phospholipid and **cholesterol** that were reduced slightly for Delta5-6A-I and greatly for Delta4-5A-I. We conclude from these findings that amino acids (aa) 100-143, specifically helix 4 (aa 100-121), contributes to the maturation of HDL through a role in lipid binding and that the downstream sequence (aa 144-186) centered around helix 6 (aa 144-165) is responsible for the activation of lecithin-**cholesterol** acyltransferase.

L25 ANSWER 12 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:233772 HCAPLUS
DOCUMENT NUMBER: 130:262129
TITLE: Apolipoprotein A-I .alpha.-helical peptide analogs as agonists for treatment of dyslipidemias
INVENTOR(S): Dasseux, Jean-Louis; Sekul, Renate; Buttner, Klaus; Cornut, Isabelle; Metz, Gunther; Dufourcq, Jean
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9916409	A2	19990408	WO 1998-US20329	19980928

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,

Search completed by David Schreiber 308-4292

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6518412	B1	20030211	US 1997-940136	19970929
CA 2304814	AA	19990408	CA 1998-2304814	19980928
EP 1039934	A1	20001004	EP 1998-950742	19980928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 503720	A	20021025	NZ 1998-503720	19980928
NO 2000001601	A	20000526	NO 2000-1601	20000328

PRIORITY APPLN. INFO.: US 1997-940136 A 19970929
WO 1998-US20329 W 19980928

OTHER SOURCE(S): MARPAT 130:262129

AB Analogs of the .alpha.-helical peptides of apolipoprotein A-I (ApoA-I) that can act as ApoA-I agonists or superagonists with many at least as active as wild-type ApoA-I are described for use in treatment of dyslipidemias. Genes for these peptides may be used in gene therapy (no data). Detail physicochem. requirements for the amphipathic .alpha.-helixes are given and these are quite different from the prior art understanding of the properties of amphipathic .alpha.-helixes of ApoA-I. A series of >250 amphipathic peptides were tested for their ability to activate LCAT. One of these peptides was found to stimulate the formation of HDL with incorporation of cholesterol.

L25 ANSWER 13 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:675296 HCAPLUS
DOCUMENT NUMBER: 132:105730
TITLE: High density lipoprotein receptors
AUTHOR(S): Fidge, Noel H.
CORPORATE SOURCE: Baker Medical Research Institute, Melbourne, 8008, Australia
SOURCE: Advances in Vascular Biology (1999), 5(Plasma Lipids and Their Role in Disease), 139-164
CODEN: AVBIFD; ISSN: 1072-0618
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with many refs. Identification of putative high d. lipoprotein receptors has been difficult, probably due to the complex nature of the ligand, HDL. Several HDL binding proteins, quite disparate in structure, have been cloned and their role in HDL metab. is currently being assessed. High d. lipoprotein binding protein, HBP, was found to lack a transmembrane domain and was assumed to be anchored to the cell surface. Although responsive to cell **cholesterol** levels, the physiol. significance of HBP has not been established. SR-B1, a member of the class B scavenger receptors is the most studied HDL receptor. The level of SR-B1 expression correlates with both **cholesterol** efflux from cells and the selective transfer into cells of **cholesteryl** ester. Its mechanism probably involves a docking process whereby HDL is anchored at the cell surface for lipid exchanges. SR-B1, like all scavenger receptors, exhibits broad ligand specificity. However it appears to be regulated by the action of pituitary hormones that stimulate steroidogenesis, and may play an important role in supplying precursor **cholesterol** for steroid hormone prodn. HB2, one of a pair of liver HDL binding proteins has been cloned. It shows high sequence homol. with adhesion mols., particularly ALCAM. When HB2 is overexpressed in cells, HDL binding increases. In macrophages, HB2 expression is down

regulated by **cholesterol** loading. The nature of the ligands recognized by the HDL receptors remains controversial, particularly their affinity for apoAI vs. apoAI/AII rich HDL particles. Identification of receptor binding domains in **apoAI** and the involvement of repeated **amphipathic** .alpha.-helixes in cell binding is also discussed. More recent evidence for post-receptor mediated cell signaling pathways offers alternative functions for HDL, some of which may not be primarily related to lipid transport. Growing evidence for the involvement of lipid free apoAI as a mediator of such pathways is also considered in this chapter.
REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 14 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1999:971734 SCISEARCH
THE GENUINE ARTICLE: 250YD
TITLE: Distinct central **amphipathic** alpha-helices in **apolipoprotein A-I** contribute to the in vivo maturation of HDL by activating LCAT (helices 5,6) and by **cholesterol** binding (helices 4,5).
AUTHOR: McManus D C (Reprint); Scott B; Frank P G; Franklin V; Marcel Y L
CORPORATE SOURCE: UNIV OTTAWA, INST HEART, OTTAWA, ON, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: CIRCULATION, (2 NOV 1999) Vol. 100, No. 18, Supp. [S], pp. 10-10.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0009-7322.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L25 ANSWER 15 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:32295 BIOSIS
DOCUMENT NUMBER: PREV200000032295
TITLE: Distinct central **amphipathic** alpha-helices in **apolipoprotein A-I** contribute to the in vivo maturation of HDL by activating LCAT (helices 5,6) and by **cholesterol** binding (helices 4,5.
AUTHOR(S): McManus, Dan C. (1); Scott, Brian (1); Frank, Phillipe G. (1); Franklin, Vivian (1); Marcel, Yves L. (1)
CORPORATE SOURCE: (1) Univ of Ottawa Heart Inst, Ottawa, ON Canada
SOURCE: Circulation, (Nov. 2, 1999) Vol. 110, No. 18 SUPPL., pp. I.2.
Meeting Info.: 72nd Scientific Sessions of the American Heart Association Atlanta, Georgia, USA November 7-10, 1999
ISSN: 0009-7322.
DOCUMENT TYPE: Conference
LANGUAGE: English

L25 ANSWER 16 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:31390 BIOSIS
DOCUMENT NUMBER: PREV200000031390
TITLE: Protection against atherosclerosis in mice by a synthetic class A **amphipathic** peptide analog of

apolipoprotein A-I.

AUTHOR(S): Garber, David W. (1); Datta, Geeta (1); Chaddha, Manjula (1); Palgunachari, M. N. (1); Garber, Matthew D. (1); Doran, Stephen F. (1); Anantharamaiah, G. M. (1)
CORPORATE SOURCE: (1) Univ of Alabama Birmingham, Birmingham, AL USA
SOURCE: Circulation, (Nov. 2, 1999) Vol. 110, No. 18 SUPPL., pp. I.538-I.539.
Meeting Info.: 72nd Scientific Sessions of the American Heart Association Atlanta, Georgia, USA November 7-10, 1999
ISSN: 0009-7322.
DOCUMENT TYPE: Conference
LANGUAGE: English

L25 ANSWER 17 OF 45 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1998234367 MEDLINE
DOCUMENT NUMBER: 98234367 PubMed ID: 9565601
TITLE: The hydrophobic face orientation of **apolipoprotein A-I amphipathic** helix domain 143-164 regulates lecithin:**cholesterol** acyltransferase activation.
AUTHOR: Sorci-Thomas M G; Curtiss L; Parks J S; Thomas M J; Kearns M W; Landrum M
CORPORATE SOURCE: Department of Pathology and Comparative Medicine, Wake Forest University School of Medicine, Winston-Salen, North Carolina 27157, USA.. msthomas@wfubmc.edu
CONTRACT NUMBER: CA12197 (NCI)
HL-43815 (NHLBI)
HL-49373 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 May 8) 273 (19) 11776-82.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980618
Last Updated on STN: 19980618
Entered Medline: 19980605

AB Apolipoprotein A-I (apoA-I) activates the plasma enzyme lecithin: **cholesterol** acyltransferase (LCAT), catalyzing the rapid conversion of lipoprotein **cholesterol** to **cholesterol** ester. Structural mutants of apoA-I have been used to study the details of apoA-I-LCAT-catalyzed **cholesterol** ester formation. Several studies have shown that the alpha-helical segments corresponding to amino acids 143-164 and 165-186 (repeats 6 and 7) are essential for LCAT activation. In the present studies, we examined how the orientation of the hydrophobic face, independent of an increase in overall hydrophobicity, affects LCAT activation. We designed, expressed, and characterized a mutant, reverse of 6 apoA-I (RO6 apoA-I), in which the primary amino acid sequence of repeat 6 (amino acids 143-164) was reversed from its normal orientation. This mutation rotates the hydrophobic face of repeat 6 approximately 80 degrees. Lipid-free RO6 apoA-I showed a marked stabilization when denatured by guanidine hydrochloride, but showed significant destabilization to guanidine hydrochloride denaturation in the lipid-bound state compared with wild-type apoA-I. Recombinant high density lipoprotein discs (rHDL) formed from RO6 apoA-I, sn-1-palmitoyl-sn-2-oleoyl phosphati-dylcholine, and **cholesterol** were approximately 12 A smaller than wild-type apoA-I rHDL. The reduced

size suggests that one of the repeats did not effectively participate in phospholipid binding and organization. The sn-1-palmitoyl-sn-2-oleoyl phosphatidylcholine RO6 rHDL were a less effective substrate for LCAT. Mapping the entire lipid-free and lipid-bound RO6 apoA-I with a series of monoclonal antibodies revealed that both the lipid-free and lipid-bound RO6 apoA-I displayed altered or absent epitopes in domains within and adjacent to repeat 6. Together, these results suggest that the proper alignment and orientation of the hydrophobic face of repeat 6 is an important determinant for maintaining and stabilizing helix-bilayer and helix-helix interactions.

L25 ANSWER 18 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1998:570531 SCISEARCH
THE GENUINE ARTICLE: 101XQ
TITLE: Studies of synthetic peptides of human **apolipoprotein A-I** containing tandem **amphipathic** alpha-helixes
AUTHOR: Mishra V K; Palgunachari M N; Datta G; Phillips M C; LundKatz S; Adeyeye S O; Segrest J P; Anantharamaiah G M (Reprint)
CORPORATE SOURCE: UNIV ALABAMA, MED CTR, DEPT MED, 1808 7TH AVE S, BIRMINGHAM, AL 35294 (Reprint); UNIV ALABAMA, MED CTR, DEPT MED, BIRMINGHAM, AL 35294; UNIV ALABAMA, MED CTR, DEPT BIOCHEM, BIRMINGHAM, AL 35294; UNIV ALABAMA, MED CTR, DEPT MOL GENET, BIRMINGHAM, AL 35294; UNIV ALABAMA, MED CTR, ATHEROSCLEROSIS RES UNIT D640, BIRMINGHAM, AL 35294; ALLEGHENY UNIV HLTH SCI, DEPT BIOCHEM, PHILADELPHIA, PA 19129
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMISTRY, (14 JUL 1998) Vol. 37, No. 28, pp. 10313-10324.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 55

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In mature human apolipoprotein A-I (apo A-I), the amino acid residues 1-43 are encoded by exon 3, whereas residues 44-243 are encoded by exon 4 of the apo A-I gene. The region encoded by exon 4 of the **apo A-I** gene contains 10 tandem **amphipathic** ct-helixes; their location and the class to which they belong are as follows: helix 1 (44-65, class Al), helix 2 (66-87, class Al), helix 3 (88-8, class Y), helix 4 (99-120, class Y), helix 5 (121-142, class Al), helix 6 (143-164, class Al), helix 7 (165-186, class Al), helix 8 (187-208, class Al), helix 9 (209-219, class Y), and helix 10 (220-241, class Y), To examine the effects of multiple tandem amphipathic helixes compared to individual helixes of apo A-I on lipid association, we have studied Lipid-associating properties of the following peptides: Ac-44-87-NH2 (peptide 1-2), Ac-66-98-NH2 (peptide 2-3), Ac-66-120-NH2 (peptide 2-3-4), Ac-88-120-NH2 (peptide 3-4), Ac-99-142-NH2 (peptide 4-5), Ac-121-164-NH2 (peptide 5-6), Ac-143-186-NH2 (peptide 6-7), Ac-165-208-NH2 (peptide 7-8), Ac-187-219-NH2 (peptide 8-9), and Ac-209-241-NH2 (peptide 9-10). To study lipid-associating properties of the region encoded by exon 3 of the apo A-I gene, 1-33-NH2 (peptide G*) has also been studied. The results of the present study indicate that, among the peptides studied, peptides 1-2 and 9-10 possess significantly higher lipid affinity than the

other peptides, with peptide 9-10 having higher lipid affinity than peptide 1-2, as evidenced by (i) higher helical content in the presence of I,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC), (ii) faster rare of association with DMPC multilamellar vesicles (MLV), (iii) greater reduction in the enthalpy of gel to liquid-crystalline phase transition of DMPC MLV, (iv) higher exclusion pressure from an egg yolk phosphatidylcholine monolayer, and (v) higher partitioning into 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine MLV. A comparison of the free energies of lipid association (Delta G) of the peptides studied here with those studied previously by us [Palgunachari, M. N., et al. (1996) Arterioscler. Thromb. Vasc. Biol, 16, 328-338] indicates that, except for the peptides 4-5 and 5-6, other peptides possess higher lipid affinities compared to constituent helixes. However, the lipid affinities of the peptides studied here are neither higher than nor equal to the sum of the lipid affinities of the constituent helixes. This indicates the absence of cooperativity among the adjacent **amphipathic** helical domains of **apo A-I** for lipid association. As indicated by ac, the lipid affinity of peptide 4-5 is higher than peptide 5 but lower than peptide 4; the lipid affinity of peptide 5-6 is lower than both peptides 5 and 6. Implications of these results for the structure and function of apo A-I are discussed.

L25 ANSWER 19 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:255216 HCAPLUS
DOCUMENT NUMBER: 129:24593
TITLE: The C-terminal helix of human apolipoprotein AII promotes the fusion of unilamellar liposomes and displaces apolipoprotein AI from high-density lipoproteins
AUTHOR(S): Lambert, Gilles; Decout, Anne; Vanloo, Berlinda; Rouy, Didier; Duverger, Nicolas; Kalopissis, Athina; Vandekerckhove, Joel; Chambaz, Jean; Brasseur, Robert; Rosseneu, Maryvonne
CORPORATE SOURCE: CJF INSERM 9508, Universite Paris VI, Paris, Fr.
SOURCE: European Journal of Biochemistry (1998), 253(1), 328-338
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To assess the functional properties of apolipoprotein (apo) AII and to investigate the mechanism leading to the displacement of apo AI from native and reconstituted high-d. lipoproteins (HDL and r-HDL) by apo AII, wild-type and variant apo AII peptides were synthesized. The wild-type peptides, residues 53-70 and 58-70, correspond to the C-terminal helix of apo AII and are predicted to insert at a tilted angle into a lipid bilayer. We demonstrate that both the apo AII-(53-70) peptide, and to a lesser extent the apo AII-(58-70) peptide are able to induce fusion of unilamellar lipid vesicles together with membrane leakage, and to displace apo AI from HDL and r-HDL. Two variants of the apo AII-(53-70)-wild-type (WT) peptide, designed either to be parallel to the water/lipid interface [apo AII-(53-70)-0.degree.] or to retain an oblique orientation [apo AII-(53-70)-30.degree.], were synthesized in order to test the influence of the obliquity on their fusogenic properties and ability to displace apo AI from HDL. The parallel variant did not bind lipids, due to its self-assocn. properties. However, the apo AII-(53-70)-30.degree. variant was fusogenic and promoted the displacement of apo AI from HDL. Moreover, the extent of fusion of the apo AII-(53-70)-WT, apo AII-(58-70)-WT and apo AII-(53-70)-30.degree. peptides was related to the .alpha.-helical content

of the lipid-bound peptides measured by IR spectroscopy. IR measurements using polarized light also confirmed the oblique orientation of the helical component of the three peptides. In native and r-HDL, the tilted insertion of the C-terminal helix of apo AII resulting in a partial destabilization of the HDL external lipid layer might contribute to the displacement of apo AI by apo AII.

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:679111 HCAPLUS
DOCUMENT NUMBER: 127:314824
TITLE: Amphipathic molecules as **cholesterol** and other lipid uptake inhibitors
INVENTOR(S): Boffelli, Dario; Hauser, Helmut
PATENT ASSIGNEE(S): Boffelli, Dario, Switz.; Hauser, Helmut
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9736927	A1	19971009	WO 1997-IB379	19970327
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2249459	AA	19971009	CA 1997-2249459	19970327
AU 9721741	A1	19971022	AU 1997-21741	19970327
AU 710061	B2	19990909		
EP 889906	A1	19990113	EP 1997-914509	19970327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1216995	A	19990519	CN 1997-194265	19970327
JP 2000509020	T2	20000718	JP 1997-535088	19970327
NZ 331980	A	20000929	NZ 1997-331980	19970327
NO 9804524	A	19981130	NO 1998-4524	19980928
US 2001005714	A1	20010628	US 1998-162095	19980928
KR 2000005408	A	20000125	KR 1998-708140	19980929

PRIORITY APPLN. INFO.: GB 1996-6686 A 19960329
GB 1996-26920 A 19961224
WO 1997-IB379 W 19970327

OTHER SOURCE(S): MARPAT 127:314824

AB **Cholesterol** biosynthesis can be inhibited by suitable inhibitors, such as the statins. However, **hypercholesterolemia**, whether familial or diet-induced, and more generally hyperlipidemia are not adequately addressed by **cholesterol** biosynthesis inhibitors alone, since the body's **cholesterol** is acquired by uptake from the diet as well as by endogenous synthesis. Lipid is also taken up from the gut. This problem is addressed by providing one or more mols. having amphipathic regions to inhibit the uptake of **cholesterol**, and other lipids, from the gut. Obesity may also be treated or prevented in

this way, as may atherosclerosis. Examples of suitable mols. having amphipathic regions include natural or variant apoproteins and other proteins and peptides having an amphipathic .alpha.-helix composed of at least about 15 amino acids. Apoproteins A-1, A-2, A-4, C-1, C-2, C-3 and E, as well as an 18-residue peptide forming an amphipathic .alpha.-helix of class A which mimics some properties of apoA-1, were shown to inhibit **cholesterol** uptake by brush border membrane vesicles.

L25 ANSWER 21 OF 45 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1998022760 MEDLINE
DOCUMENT NUMBER: 98022760 PubMed ID: 9354635
TITLE: The helix-hinge-**helix** structural motif in human **apolipoprotein A-I** determined by NMR spectroscopy.
AUTHOR: Wang G; Sparrow J T; Cushley R J
CORPORATE SOURCE: Institute of Molecular Biology and Biochemistry, Simon Fraser University, Burnaby, British Columbia, Canada V5A 1S6.
SOURCE: BIOCHEMISTRY, (1997 Nov 4) 36 (44) 13657-66.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1GW3; PDB-1GW4; PDB-R1GW3MR; PDB-R1GW4MR
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971204

AB The conformation of a synthetic peptide of 46 residues from apoA-I was investigated by fluorescence, CD, and 2D NMR spectroscopies in lipid-**mimetic** environments. ApoA-I(142-187) is mainly unstructured in water but helical in SDS or dodecylphosphocholine (DPC), although the peptide only associates with DPC at approximately the critical micellar concentration. Solution structures of apoA-I(142-187) were determined by distance geometry calculations based on 450 (in DPC-d38) or 397 (in SDS-d25) NOE-derived distance restraints, respectively. Backbone RMSDs for superimposing the two helical regions 146-162 and 168-182 are 0.98 +/- 0.22 (2.38 +/- 0.20) and 1.99 +/- 0.42 (2.02 +/- 0.21) A in DPC (SDS), respectively. No interhelical NOE was found, suggesting that helix-helix interactions between the two helical domains in apoA-I(142-187) are unlikely. Similar average, curved helix-hinge-helix structures were found in both SDS and DPC micelles with the hydrophobic residues occupying the concave face, indicating that hydrophobic interactions dominate. Intermolecular NOESY experiments, performed in the presence of 50% protonated SDS, confirm that the two amphipathic helices and Y166 in the hinge all interact with the micelle. The involvement of Y166 in lipid binding is supported by fluorescence spectroscopy as well. On the basis of all the data above, we propose a model for the peptide-lipid complexes wherein the curved amphipathic helix-hinge-helix structural motif straddles the micelle. The peptide-aided signal assignment achieved for apoA-I(122-187) (66mer) and apoA-I suggests that such a structural motif is retained in the longer peptide and most likely in the intact protein.

L25 ANSWER 22 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 97:821159 SCISEARCH
THE GENUINE ARTICLE: YD848
TITLE: Predicting the structure of apolipoprotein A-1 in reconstituted high-density lipoprotein disks

AUTHOR: Phillips J C; Wriggers W; Li Z G; Jonas A; Schulten K (Reprint)
CORPORATE SOURCE: UNIV ILLINOIS, BECKMAN INST 3147, DEPT PHYS, COLL MED, 405 N MATHEWS AVE, URBANA, IL 61801 (Reprint); UNIV ILLINOIS, BECKMAN INST 3147, DEPT PHYS, COLL MED, URBANA, IL 61801; UNIV ILLINOIS, COLL MED, DEPT BIOCHEM, URBANA, IL 61801
COUNTRY OF AUTHOR: USA
SOURCE: BIOPHYSICAL JOURNAL, (NOV 1997) Vol. 73, No. 5, pp. 2337-2346.
Publisher: BIOPHYSICAL SOCIETY, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0006-3495.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 54
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In reconstituted high-density lipoproteins, apolipoprotein A-I and phosphatidylcholines combine to form disks in which the **amphipathic** alpha-helices of **apolipoprotein A-1** bind to the edge of a lipid bilayer core, shielding the hydrophic lipid tails from the aqueous environment. We have employed experimental data, sequence analysis, and molecular modeling to construct an atomic model of such a reconstituted high-density lipoprotein disk consisting of two apolipoprotein A-I proteins and 160 palmitoyloleoylphosphatidylcholine lipids. The initial globular domain (1-47) of apolipoprotein A-I was excluded from the model, which was hydrated with an 8-Angstrom shell of water molecules. Molecular dynamics and simulated annealing were used to test the stability of the model. Both head-to-tail and head-to-head forms of a reconstituted high-density lipoprotein were simulated, In our simulations the protein contained and adhered to the lipid bilayer while providing good coverage of the lipid tails.

L25 ANSWER 23 OF 45 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 97226212 MEDLINE
DOCUMENT NUMBER: 97226212 PubMed ID: 9102180
TITLE: Design of a new class of amphipathic helical peptides for the plasma apolipoproteins that promote cellular **cholesterol** efflux but do not activate LCAT.
AUTHOR: Labeur C; Lins L; Vanloo B; Baert J; Brasseur R; Rosseneu M
CORPORATE SOURCE: Innogenetics NV, Gent, Belgium.. christine.labeur@rug.ac.be
SOURCE: ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (1997 Mar) 17 (3) 580-8.
Journal code: 9505803. ISSN: 1079-5642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970424
Last Updated on STN: 19980206
Entered Medline: 19970415

AB Amphipathic helical peptides represent the lipid-binding units of the soluble plasma apolipoproteins. Several synthetic peptide analogues have been designed to mimic such structures and have been used to unravel some of the mechanisms involved in the physiological function of the apolipoproteins, including lipid binding, LCAT activation, and enhancement of **cholesterol** efflux from lipid-laden cells. A series of novel

synthetic peptides, named ID peptides, was modeled on the basis of the structural properties common to the **amphipathic** helices of apolipoprotein (**apo**) **A-I**. In these new peptides, however, the segregation between hydrophobic and hydrophilic faces of the helices is more pronounced than in apoA-I, so that the surface of the hydrophobic and hydrophilic faces of the amphipathic helices is equal. Moreover, there are fewer negatively charged residues in the center of the hydrophilic face of the helical peptides. Most charged amino acids are located along the edge of the helix and are susceptible to forming salt bridges with residues of an antiparallel helix, such as around a discoidal phospholipid/peptide complex. The physicochemical characteristics of these peptides and their complexes with phospholipids were compared with those of the 18A peptide and its lipid/peptide complex. All ID peptides bind dimyristoylphosphatidylcholin e vesicles more rapidly than the 18A peptide to yield discoidal peptide/phospholipid complexes of comparable size. The alpha-helical content of the lipid-free ID peptides is close to that of the 18A peptide and increases slightly on lipid binding. The stability of the ID and 18A peptides and of the phospholipid/peptide complexes against guanidinium hydrochloride denaturation is higher than that of lipid-free and lipid-bound apoA-I. LCAT activation by the 18A/phospholipid/ **cholesterol** complexes equals that of apoA-I/ phospholipid/ **cholesterol** complexes, whereas none of the ID peptides tested is able to activate LCAT to a significant extent. Incubation of the peptide/phospholipid complexes with lipid-laden macrophages induces cellular **cholesterol** efflux and incorporation of **cholesterol** into the complexes. The **cholesterol** efflux capacity of the peptide/phospholipid complexes is comparable among the peptides and higher than that of apoprotein/phospholipid complexes. In conclusion, although the amphipathicity of the new peptides is higher than that of the 18A model peptide, the lack of LCAT activation by the ID peptides suggests that an enhanced segregation of the hydrophobic and hydrophilic residues, equal magnitude of hydrophobic and hydrophilic faces of the helix, and the absence of negatively charged residues in the central part of the hydrophilic face might account for the lack of LCAT activity of these peptides. These parameters do not affect the capacity of the peptide/phospholipid complexes to promote cellular **cholesterol** efflux.

L25 ANSWER 24 OF 45 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 97260903 MEDLINE
DOCUMENT NUMBER: 97260903 PubMed ID: 9113723
TITLE: Structure of apo A-I high-density lipoproteins: a review.
AUTHOR: Titov V N
CORPORATE SOURCE: Cardiology Research Center, Russian Academy of Medical Sciences, Moscow, Russia.
SOURCE: BIOCHEMISTRY, (1997 Jan) 62 (1) 1-14. Ref: 73
Journal code: 0376536. ISSN: 0006-2979.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 19970514
Entered Medline: 19970508
AB Current models of high-density lipoprotein (LP) are reviewed on the basis

of physicochemical protein-lipid interactions. The micellar model of LP fails to explain the transformation of micelles into disk-shaped particles and gives an indefinite number of apo A-I molecules in the surface monolayer. Micellar structure fails to explain how changes in the conformation of apoprotein affect the structure and function of high-density LP. The phospholipid bilayer encircled by apoprotein model does not explain the accepting of nonpolar **cholesterol** esters by high-density LP. The transformation of a bilayer phospholipid disk into a spherical structure is unclear. Since the structure and function of LP are determined by their protein chemistry, an alternative model of high-density LP as a protein-lipid disk is developed. Apo A-I bound with polar phospholipids forms a planar amphipathic disk. Phospholipids containing the more hydrophobic polyene acids are structured by apo A-I in the monolayer on the hydrophobic side of the disk. The less unsaturated polyene acids are structured by apo A-I in the multi-lamellar phase of phospholipid bilayers on the hydrophilic side of the disk. The lateral surface of the disk is formed by hydrophilic domains of apo A-I. Each apo A-I molecule forms a separate LP. Polyene fatty acids are esterified with **cholesterol** by lecithin-**cholesterol** acyltransferase on the hydrophobic side of the disk. The **cholesterol**-esterified polyene acids are accepted here also in association with hydrophobic groups of amino acid residues of apo A-I. Interaction with nonpolar **cholesterol** esters changes the conformation of apo A-I, forming a cylindrical structure from the planar protein-lipid disk. The lateral surface of the cylinder is formed by the same hydrophilic domains of apo A-I as in the disk-shaped particle. However, the alpha-helices of these domains are arranged perpendicularly to the acyl chains of the phospholipids in the disk but in parallel in the cylinder. The interaction of apo A-I protein-lipid disks by loop domains on the lateral surfaces results in the formation of large disk-shaped structures which are specific for a low-activity lecithin-**cholesterol** acyltransferase. The interaction of loop domains of cylindrical high-density LP produces hexagonal structures. The heterogeneity of apo A-I LP is caused by the conformation of the apoprotein which depends on the medium: the native conformation in the hydrated medium, the intermediate conformation in association with polar phospholipids, and the final conformation in association with phospholipids and nonpolar **cholesterol** esters. Functional features of LP depend on the conformation of apo A-I. The active and passive transport of polyene fatty acids to cells is based on the accumulation of phospholipids of different hydrophobicity on the appropriate sides of the **apo A-I amphipathic** disk.

L25 ANSWER 25 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1996:590709 HCAPLUS
DOCUMENT NUMBER:	125:241030
TITLE:	Apolipoprotein A-I structural modification and the functionality of reconstituted high density lipoprotein particles in cellular cholesterol efflux
AUTHOR(S):	Gillotte, Kristin L.; Davidson, W. Sean; Lund-Katz, Sissel; Rothblat, George H.; Phillips, Michael C.
CORPORATE SOURCE:	Dep. Biochem., Allegheny Univ. Health Sci., Philadelphia, PA, 19129, USA
SOURCE:	Journal of Biological Chemistry (1996), 271(39), 23792-23798 CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER:	American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE:	Journal

Search completed by David Schreiber 308-4292

LANGUAGE: English

AB The role of HDL and its major protein constituent, apolipoprotein (apo) A-I, in promoting the removal of excess cholesterol from cultured cells has been well established; however, the mechanisms by which this occurs are not completely understood. To address the effects of apoA-I modification on cellular unesterified (free) cholesterol (**FC**) efflux, three recombinant human apoA-I deletion mutants and plasma apoA-I were combined with 1-palmitoyl-2-oleoylphosphatidylcholine (POPC) and **FC** to make reconstituted high d. lipoprotein (rHDL) discoidal complexes. These particles were characterized structurally and for their efficiency as acceptors of mouse L-cell fibroblast cholesterol. The deletion mutant proteins lacked N-terminal (apoA-I (.DELTA.44-126)), central (apoA-I (.DELTA.139-170)), or C-terminal (apoA-I (.DELTA.190-243)) domains of apoA-I. The three deletion mutants all displayed lipid-binding abilities and formed discoidal complexes that were similar in major diam. (13.2 nm) to those formed by human apoA-I when reconstituted at a 100:5:1 (POPC:**FC**: protein) mole ratio. Gel filtration profiles indicated unreacted protein in the prepn. made with apoA-I (.DELTA.190-243), which is consistent with the C-terminus portion of apoA-I being an important determinant of lipid binding. Measurements of the percent .alpha.-helix content of the proteins, as well as the no. of protein mols. per rHDL particle, gave an indication of the arrangement of the deletion mutant proteins in the discoidal complexes. The rHDL particles contg. the deletion mutants had more mols. of protein present than particles contg. intact apoA-I, to the extent that a similar no. of helical segments was incorporated into each of the discoidal species. Comparison of the exptl. detd. no. of helical segments with an est. of the available space indicated that the deletion mutant proteins are probably more loosely arranged than apoA-I around the edge of the rHDL. The abilities of the complexes to remove radiolabeled **FC** were compared in expts. using cultured mouse L-cell fibroblasts. All four discoidal complexes displayed similar abilities to remove **FC** from the plasma membrane of L-cells when compared at an acceptor concn. of 50 .mu.g of phospholipid/mL. Thus, none of the deletions imposed in this study notably altered the ability of the rHDL particles to participate in cellular **FC** efflux. These results suggest that efficient apoA-I-mediated **FC** efflux requires the presence of amphipathic .alpha.-helical segments but is not dependent on specific helical segments.

L25 ANSWER 26 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 96:142108 SCISEARCH

THE GENUINE ARTICLE: TV417

TITLE: ONLY THE 2 END HELIXES OF 8 TANDEM **AMPHIPATHIC** HELICAL DOMAINS OF HUMAN **APO A-I** HAVE SIGNIFICANT LIPID AFFINITY - IMPLICATIONS FOR HDL ASSEMBLY

AUTHOR: PALGUNACHARI M N; MISHRA V K; LUNDKATZ S; PHILLIPS M C; ADEYEYE S O; ALLURI S; ANANTHARAMAIAH G M (Reprint); SEGREST J P

CORPORATE SOURCE: UAB, MED CTR, DEPT MED, BIRMINGHAM, AL, 35294 (Reprint); UAB, MED CTR, DEPT MED, BIRMINGHAM, AL, 35294; UAB, MED CTR, DEPT BIOCHEM, BIRMINGHAM, AL, 35294; UAB, MED CTR, DEPT MOLEC GENET, BIRMINGHAM, AL, 35294; UAB, MED CTR, ATHEROSCLEROSIS RES UNIT, BIRMINGHAM, AL, 35294; MED COLL PENN, DEPT BIOCHEM, PHILADELPHIA, PA, 19129; HAHNEMANN UNIV, PHILADELPHIA, PA, 19102

COUNTRY OF AUTHOR: USA

SOURCE: ARTERIOSCLEROSIS THROMBOSIS AND VASCULAR BIOLOGY, (FEB

1996) Vol. 16, No. 2, pp. 328-338.
ISSN: 1079-5642.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 50

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human apolipoprotein A-I (ape A-I) possesses multiple tandem repeating 22-mer amphipathic alpha-helixes. Computer analysis and studies of model synthetic peptides and recombinant protein-lipid complexes of phospholipids have suggested that apo A-I interacts with HDL surface lipids through cooperation among its individual amphipathic helical domains. To delineate the overall lipid-associating properties of apo A-I, the first step is to understand the lipid-associating properties of individual amphipathic helical domains. To this end, we synthesized and studied each of the eight tandem repeating 22-mer domains of apo A-I: residues 44-65, 66-87, 99-120, 121-142, 143-164, 165-186, 187-208, and 220-241. Among the 22-mers, only the N- and C-terminal peptides (44-65 and 220-241) were effective in clarifying multilamellar vesicles (MLVs) of dimyristoylphosphatidylcholine (DMPC). These two peptides also exhibited the highest partition coefficient into 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylcholine liposomes, the highest exclusion pressure for penetration into an egg yolk phosphatidylcholine monolayer, and the greatest reduction in the enthalpy of the gel-to-liquid crystalline phase transition of DMPC MLVs. These results suggest that the strong, lipid-associating properties of apo A-I are localized to the N- and C-terminal amphipathic domains. Although each of the eight peptides studied has an amphipathic structure, models based on changes in residual effective amino acid hydrophobicity resulting from differing depths of helix penetration into the lipid are best able to explain the high lipid affinity possessed by the two terminal domains. Differential scanning calorimetry (DSC) studies showed that on a molar basis, apo A-I is about 10 times more effective than the most effective peptide analyzed in reducing the enthalpy of the gel-to-liquid crystalline phase transition of DMPC MLVs. Because previous proteolysis experiments coupled with the present DSC results suggest that the lipid-associating domains of apo A-I are distributed throughout the length of the 243 amino acid residues, we propose that the terminal amphipathic helical domains are involved in the initial binding of apo A-I to the lipid surface to form HDL particles, followed by cooperative binding of the middle six amphipathic helical domains, perhaps aided by salt-bridge formation between adjacent helixes arranged in an antiparallel orientation.

L25 ANSWER 27 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 95:835935 SCISEARCH
THE GENUINE ARTICLE: TH008

TITLE: APOLIPOPROTEIN-A-I STIMULATES PLACENTAL-LACTOGEN EXPRESSION BY HUMAN TROPHOBLAST CELLS

AUTHOR: HANDWERGER S (Reprint); MYERS S; RICHARDS R; RICHARDSON B; TURZAI L; MOEYKINS C; MEYER T; ANANTHARAMAHIAH G M
CORPORATE SOURCE: CHILDRENS HOSP, MED CTR, DIV ENDOCRINOL, 3333 BURNETT AVE, CINCINNATI, OH, 45229 (Reprint); CHILDRENS HOSP, MED CTR, PERINATAL RES INST, CINCINNATI, OH, 45229; UNIV CINCINNATI, COLL MED, DEPT PEDIAT, CINCINNATI, OH, 45229; UNIV ALABAMA, DEPT MED, ATHEROSCLEROSIS RES UNIT, BIRMINGHAM, AL, 35294
COUNTRY OF AUTHOR: USA

SOURCE: ENDOCRINOLOGY, (DEC 1995) Vol. 136, No. 12, pp. 5555-5560.
ISSN: 0013-7227.

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 24
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Earlier studies from our laboratory indicated that apolipoprotein A-I(Apo A-I) stimulates the acute release of human placental lactogen (hPL) from trophoblast cells in culture. We have now demonstrated that Apo A-I also causes a secondary increase in hPL release, beginning about 6 h after exposure to Apo A-I, that is blocked by cyclo-heximide and actinomycin D. Apo A-I also stimulated a dose-dependent increase in hPL promoter activity in JAR cells transfected with a 1.1-kilobase (-1078/2) fragment of the hPL(3) promoter coupled to a chloramphenicol acetyltransferase (CAT) reporter gene. Maximal stimulation, 5.2-fold above basal levels, occurred at an Apo A-I concentration of 1.5 mg/ml, which is within the physiological concentration of **Apo A-I** during pregnancy. 37pA, a synthetic **amphipathic** peptide that mimics the secondary structure of Apo A-I and stimulates the synthesis and release of hPL, also stimulated a dose-dependent increase in CAT activity, with maximal stimulation comparable to that caused by Apo A-I. In addition, Apo A-I stimulated a modest increase in CAT activity in BeWo choriocarcinoma cells, Chinese hamster ovary cells, and HeLa cells. However, the maximal stimulation of hPL promoter activity in the Chinese hamster ovary and HeLa cells (similar to 2.5-fold above basal levels) was less than that in choriocarcinoma cells, suggesting that trophoblast cell nuclear factors may be necessary for maximal expression of the promoter in response to Apo A-I. Taken together, these results indicate that Apo A-I stimulates hPL gene expression, and that DNA elements in the first 1.1 kilobase of the promoter are sufficient for transactivation by Apo A-I.

L25 ANSWER 28 OF 45 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 94364988 MEDLINE
DOCUMENT NUMBER: 94364988 PubMed ID: 8083197
TITLE: The influence of apolipoprotein structure on the efflux of cellular free cholesterol to high density lipoprotein.
AUTHOR: Davidson W S; Lund-Katz S; Johnson W J; Anantharamaiah G M; Palgunachari M N; Segrest J P; Rothblat G H; Phillips M C
CORPORATE SOURCE: Medical College of Pennsylvania, Department of Biochemistry, Philadelphia 19129.
CONTRACT NUMBER: HL07443 (NHLBI)
HL22633 (NHLBI)
HL34343 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Sep 16) 269 (37) 22975-82.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941021
Last Updated on STN: 19980206
Entered Medline: 19941011

AB The influence of apolipoprotein conformation on the ability of high density lipoprotein (HDL) to remove cellular free cholesterol (**FC**) has not been studied in detail. To address the effects of amphipathic alpha-helix structure on cellular **FC** efflux, three class A **helical** peptides and apolipoprotein (**apo**) **AI** were complexed to dimyristoyl phosphatidylcholine (DMPC) to make discoidal

complexes that were used as acceptors of cell cholesterol. The peptides consisted of an 18-amino acid, amphipathic, alpha-helical peptide with the sequence DWLKAFYDKVAEKLKEAF (18A), a dimer of 18A covalently linked by a proline residue (37pA), and acetyl-18A-amide (Ac-18A-NH2) that has a higher alpha-helix content than the unblocked 18A molecule. The three peptides strongly mimic the lipid-binding characteristics of the amphipathic segments of apolipoproteins and form discoidal complexes with DMPC that are similar in diameter (11-12 nm) to those formed by human apoAI when reconstituted at a 2.5:1 (w:w) phospholipid to protein ratio. The abilities of these complexes to remove radiolabeled **FC** were compared in experiments using cultured mouse L-cell fibroblasts; efflux of **FC** from both the plasma membrane and the lysosomal pools was examined. For each of the acceptors, the removal of cholesterol from the plasma membrane and lysosomal pools was equally efficient. All four discoidal complexes were equally efficient cell membrane **FC** acceptors when compared at saturating acceptor concentrations of > 200 micrograms of DMPC/ml of medium. However, at the same lipid concentration, protein-free DMPC small unilamellar vesicles (SUV) were significantly less efficient. The initial rates of **FC** removal from cells at saturating concentrations of acceptor particles (Vmax) were 12, 10, 10, and 11% per h, respectively, for the complexes containing either 18A, Ac-18A-NH2, 37pA, or apoAI, but only 1% cellular **FC** per h for the DMPC SUV. The 10-fold higher Vmax for the apoprotein/peptide-containing acceptors was likely due to a reversible interaction of apoprotein or peptide with the plasma membrane that changed the lipid packing characteristics in such a way as to increase the rate of **FC** desorption from the cell surface. This interaction required amphipathic alpha-helical segments, but it was not affected by the length, number, or lipid-binding affinity of the helices. Furthermore, the efflux efficiency was not dependent on the amino acid sequence of the helical segments which suggests that this interaction is not mediated by a specific cell surface binding site.(ABSTRACT TRUNCATED AT 400 WORDS)

L25 ANSWER 29 OF 45 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 95015043 MEDLINE
DOCUMENT NUMBER: 95015043 PubMed ID: 7929849
TITLE: Synthetic **amphipathic** helical peptides that mimic **apolipoprotein A-I** in clearing cellular **cholesterol**.
AUTHOR: Mendez A J; Anantharamaiah G M; Segrest J P; Oram J F
CORPORATE SOURCE: Department of Medicine RG-26, University of Washington, Seattle 98195.
CONTRACT NUMBER: HL-18645 (NHLBI)
HL-31194 (NHLBI)
HL-34343 (NHLBI)
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1994 Oct) 94 (4) 1698-705.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19980206
Entered Medline: 19941110

AB Clearance of excess **cholesterol** from cells by HDL is facilitated by the interaction of HDL apolipoproteins with cell-surface binding sites or receptors, a process that may be important in preventing

atherosclerosis. In this study, synthetic peptides containing 18-mer amphipathic helices of the class found in HDL apolipoproteins (class A) were tested for their abilities to remove **cholesterol** and phospholipid from cultured sterol-laden fibroblasts and macrophages and to interact with cell-surface HDL binding sites. Lipid-free peptides containing two identical tandem repeats of class A amphipathic helices promoted **cholesterol** and phospholipid efflux from cells and depleted cellular **cholesterol** accessible for esterification by acyl CoA/**cholesterol** acyltransferase, similar to what was observed for purified apolipoprotein A-I. Peptide-mediated removal of plasma membrane **cholesterol** and depletion of acyl CoA/ **cholesterol** acyltransferase-accessible **cholesterol** appeared to occur by separate mechanisms, as the latter process was less dependent on extracellular phospholipid. The dimeric amphipathic helical peptides also competed for high-affinity HDL binding sites on **cholesterol**-loaded fibroblasts and displayed saturable high-affinity binding to the cell surface. In contrast, peptides with a single helix had little or no ability to remove cellular **cholesterol** and phospholipid, or to interact with HDL binding sites, suggesting that cooperativity between two or more helical repeats is required for these activities. Thus, synthetic peptides comprising dimers of a structural motif common to exchangeable apolipoproteins can mimic apolipoprotein A-I in both binding to putative cell-surface receptors and clearing **cholesterol** from cells.

L25 ANSWER 30 OF 45 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 94:503051 SCISEARCH
THE GENUINE ARTICLE: PB435
TITLE: STRUCTURAL AND FUNCTIONAL-PROPERTIES OF HUMAN AND MOUSE APOLIPOPROTEIN-A-I
AUTHOR: GONG E L (Reprint); TAN C S; SHOUKRY M I; RUBIN E M; NICHOLS A V
CORPORATE SOURCE: UNIV CALIF BERKELEY, LAWRENCE BERKELEY LAB, DIV LIFE SCI, BERKELEY, CA, 94720 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA-LIPIDS AND LIPID METABOLISM, (04 AUG 1994) Vol. 1213, No. 3, pp. 335-342.
ISSN: 0005-2760.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 31

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Mouse and human plasma apolipoprotein A-I (apo A-I-m and apo A-I-h, respectively) were investigated to compare their molecular properties in solution, their incorporation into palmitoyloleoylphosphatidylcholine-apo A-I (POPC-apo A-I) discoidal complexes, their structural stability in discoidal complexes and high-density lipoproteins (HDL), and their effect on structural rearrangement of discoidal complexes upon interaction with low-density lipoproteins (LDL). Unlike apo A-I-h, only minimal concentration-dependent self-association was observed for apo A-I-m. While both apo A-I-m and apo A-I-h formed discoidal complexes of distinct composition and size that reflected reassembly molar ratios of POPC/apo A-I, apo A-I-m demonstrated specific deficiencies in formation of larger-sized complexes. Denaturation of both apo A-I-m or apo A-I-h-containing complexes and HDL with guanidine hydrochloride (GuHCl) indicated significantly reduced stabilization of apo A-I-m by lipid in these particles. Interaction of apo A-I-m- or apo A-I-h-containing discoidal complexes with human plasma LDL revealed a more extensive

conversion of apo A-I-m-complexes to smaller species. Mean hydrophobicities and mean hydrophobic moments of **amphipathic** helical segments in **apo A-I**-m and apo A-I-h were compared; differences potentially contributing to differential lipid-binding properties between apo A-I-m and apo A-I-h were identified. Our results demonstrate differences between apo A-I-m and apo A-I-h that may contribute to the major changes in plasma HDL distribution and function observed in apo A-I-h transgenic mice.

L25 ANSWER 31 OF 45 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 93131896 MEDLINE
DOCUMENT NUMBER: 93131896 PubMed ID: 8420935
TITLE: The number of **amphipathic** alpha-helical segments of **apolipoproteins A-I**, E, and A-IV determines the size and functional properties of their reconstituted lipoprotein particles.
AUTHOR: Jonas A; Steinmetz A; Churgay L
CORPORATE SOURCE: Department of Biochemistry, College of Medicine, University of Illinois, Urbana 61801.
CONTRACT NUMBER: HL-16059 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Jan 25) 268 (3) 1596-602.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 19930226
Last Updated on STN: 19980206
Entered Medline: 19930218

AB The objective of this work was to determine the role of the amphipathic alpha-helical structural units of human apolipoproteins A-I, E, and A-IV in defining the sizes and reactivities with lecithin:**cholesterol** acyltransferase (LCAT) of their reconstituted lipoprotein particles. We prepared reconstituted high density lipoprotein (rHDL) particles with each of the three apolipoproteins in two weight ratios with lipid: 2.7/0.07/1 and 1.35/0.04/1, palmitoyloleoylphosphatidylcholine/**cholesterol** /apolipoprotein, by the sodium cholate dialysis procedure; and examined the rHDL product sizes and distributions by nondenaturing gradient gel electrophoresis. The rHDL particles were also incubated with low density lipoprotein (LDL), and with LDL plus LCAT, to observe any structural modifications due to phospholipid transfers to LDL and to **cholesterol** esterification by LCAT. In addition, we examined the average structural properties of the original rHDL by several fluorescence methods and circular dichroism spectroscopy, and determined their reaction kinetics with LCAT. The results indicate that the diameters of the largest rHDL particles, containing two apolipoproteins per particle, correlate with the maximum number of putative amphipathic alpha-helical segments in their sequences, and that smaller particles of this class may arise from the removal of one or more alpha-helical segments from contact with lipid. Furthermore, the larger particles may be converted into the smaller ones upon loss of phospholipid to LDL, and may form one or two well defined products when reacted with LCAT. In general, the subclasses of particles have distinct spectroscopic properties, consistent with a different apolipoprotein folding in particles containing different proportions of phospholipid to apolipoprotein. Furthermore, the different apolipoprotein structures lead to significant differences in reactivity with LCAT.

L25 ANSWER 32 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:619806 HCAPLUS
DOCUMENT NUMBER: 119:219806
TITLE: Effect of end group blockage on the properties of a class A amphipathic helical peptide
AUTHOR(S): Venkatachalapathi, Y. V.; Phillips, Michael C.; Epand, Richard M.; Epand, Raquel F.; Tytler, Ewan M.; Segrest, Jere P.; Anantharamaiah, G. M.
CORPORATE SOURCE: Sch. Med., Univ. Alabama, Birmingham, AL, 35294, USA
SOURCE: Proteins: Structure, Function, and Genetics (1993), 15(4), 349-59
CODEN: PSFGEY; ISSN: 0887-3585
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a recent classification of biol. active amphipathic .alpha.-helixes, the lipid-assocg. domains in exchangeable plasma apolipoproteins have been classified as class A amphipathic helixes. A model peptide analog with the sequence, Asp Trp Leu Lys Ala Phe Tyr Asp Lys Val Ala Glu Lys Leu Lys Glu Ala Phe (18A), possesses the characteristics of a class A amphipathic helix. The addn. of an acetyl group at the .alpha.-amino terminus and an amide at the .alpha.-carboxyl terminus, to obtain Ac-18A-NH2, produces large increases in helicity for the peptide both in soln. and when assocd. with lipid (for 18A vs Ac-18A-NH2, from 6 to 38% helix in buffer and from 49 to 92% helix when bound to dimyristoylphosphatidylcholine in discoidal complexes). Blocking of the end-groups of 18A stabilizes the .alpha.-helix in the presence of lipid by approx. 1.3 kcal/mol. There is also an increase in the self-assocn. of the blocked peptide in aq. soln. The free energy of binding to the PC-water interface is increased only by about 3% (from -8.0 kcal mol for 18A to -8.3 kcal/mol for Ac-18A-NH2). The Ac-18A-NH2 has a much greater potency in raising the bilayer to hexagonal phase transition temp. of palmitoyloleoylphosphatidylethanolamin e than does 18A. In this regard Ac-18A-NH2 more closely resembles the behavior of the apolipoprotein A-I, which is the major protein component of high-d. lipoprotein and a potent inhibitor of lipid hexagonal phase formation. The activation of the plasma enzyme lecithin: **cholesterol** acyltransferase by the Ac-18A-NH2 peptide is greater than the 18A analog and comparable to that obsd. with the apo A-I. In the case of Ac-18A-NH2, the higher activating potency may be due, at least in part, to the ability of the peptide to micellize egg PC vesicles.

L25 ANSWER 33 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:609463 HCAPLUS
DOCUMENT NUMBER: 117:209463
TITLE: Epitope mapping of the human biliary amphipathic, anionic polypeptide: similarity with a calcium-binding protein isolated from gallstones and bile, and immunologic cross-reactivity with apolipoprotein A-I
AUTHOR(S): Domingo, N.; Grosclaude, J.; Bekaert, E. D.; Mege, D.; Chapman, M. J.; Shimizu, S.; Ayrault-Jarrier, M.; Ostrow, J. D.; Lafont, H.
CORPORATE SOURCE: Unite 130, INSERM, Marseille, 13009, Fr.
SOURCE: Journal of Lipid Research (1992), 33(10), 1419-30
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Biliary amphipathic anionic polypeptide (APF) the major protein of the pigment-lipoprotein complex in bile, and calcium-binding protein (CBP)

from gallstones are both small (<10 kDa), highly acidic, amphipathic proteins present in bile and closely assocd. also with pigmented areas in human gallstones. Polyclonal antibodies against APF have shown cross reactivity with plasma high d. lipoproteins (HDL). This study examines the hypothesis that APF and CBP might be closely related or even identical, and might also share common epitopes with the larger apoA-I (23 kDa). To assess this, immunoreactivity of the three delipidated, highly purified proteins was detd. against a panel of 12 monoclonal antibodies (MAbs) prepd. against APF and a panel of 4 MAbs against apoA-I. Western blotting of APF and CBP in 15% SDS-PAGE yielded one band with an apparent mol. wt. of 6.5 kDa, which, along with apoA-I, was immunostained by polyclonal antibodies to APF and apoA-I. Using 12 MAbs against APF with three types of ELISA (direct antigen binding, competitive antigen displacement, and epitope competition between antibodies), it was shown that APF and delipidated apoA-I shared six epitopes, three of which were detected also on the surface of intact HDL particles. Six other epitopes were present in APF but not apoA-I, four of which were exposed on the surface of HDL. Four MAbs against apoA-I reacted with APF and CBP. Amino acid analyses of APF and CBP were similar with 20-23% acidic and 7-11% basic amino acids and low contents of cysteine, methionine, and tyrosine; both differed from apoA-I in contg. isoleucine and cysteine. Using ELISA and one MAb (no. 32) against APF, this polypeptide was detected in human plasma HDL, the pigment-lipoprotein complex in the bile of humans, dogs, and rats, and in both pigment and **cholesterol** gallstones. Like CBP, APF contained tightly bound bile pigments and arrested the pptn. of calcium carbonate from a supersatd. soln. in vitro. These common properties and immunol. cross-reactivity between APF and CBP suggests that the two proteins may be identical, and likely play a role in both transport of **cholesterol** and pptn. of calcium salts in bile, and therefore in the formation of both **cholesterol** and calcium-pigment-contg. gallstones. APF/CBP also shares some epitopes with apoA-I and plasma HDL. The presence of amino acids in APF/CBP not found in apoA-I, however, renders it probable that APF is a true minor apolipoprotein of HDL, distinct from apoA-I, that binds tightly to the surface of HDL.

L25 ANSWER 34 OF 45 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 92337665 MEDLINE
DOCUMENT NUMBER: 92337665 PubMed ID: 1632797
TITLE: Apolipoprotein A-1 interacts with the N-terminal fusogenic domains of SIV (simian immunodeficiency virus) GP32 and HIV (human immunodeficiency virus) GP41: implications in viral entry.
AUTHOR: Martin I; Dubois M C; Saermark T; Ruysschaert J M
CORPORATE SOURCE: Laboratoire de Chimie-Physique des Macromolecules aux Interfaces, Universite Libre de Bruxelles, Belgium.
CONTRACT NUMBER: A1-27136-01A1
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1992 Jul 15) 186 (1) 95-101.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920904
Last Updated on STN: 19970203
Entered Medline: 19920814
AB Previous studies showed that apoA1, the major protein component of HDL

(High Density Lipoprotein), inhibited HIV **infectivity** and **virus**-induced syncytia formation. The mechanism of inhibition is unknown. We bring here evidence that the **amphipathic helices** of **apoA1** interact with the N-terminal peptides of SIV gp32 and HIV gp41. These peptides have been shown to be associated with the initial steps of the fusion between the host cell and the virus. Binding of apoA1 to these peptides prevents the insertion of the fusogenic domains into the cell membrane and inhibits the fusion and the entry of the virus into the host cell.

L25 ANSWER 35 OF 45 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 91177846 MEDLINE
DOCUMENT NUMBER: 91177846 PubMed ID: 1706710
TITLE: The **amphipathic** alpha-helical repeats of **apolipoprotein A-I** are responsible for binding of high density lipoproteins to HepG2 cells.
AUTHOR: Leblond L; Marcel Y L
CORPORATE SOURCE: Laboratory of Lipoprotein Metabolism, Clinical Research Institute of Montreal, Quebec, Canada.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Apr 5) 266 (10) 6058-67.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910519
Last Updated on STN: 19970203
Entered Medline: 19910501

AB Nine monoclonal antibodies (mAbs) against apoA-I reacting with distinct but overlapping epitopes covering more than 90% of the sequence have been used to block the interaction of 125I-labeled high density lipoprotein (125I-HDL) with HepG2 cells in order to delineate the cell binding domain of apolipoprotein A-I (apoA-I). While 2 mAbs reacting with epitopes exclusively localized in the N-terminal region (residues 1 to 86) enhanced slightly association of 125I-HDL, all other mAbs, which react with epitopes localized in the regions of amphipathic alpha-helical repeats, inhibited that association by 9 to 15%. Although this inhibition is not significant compared to the effect of an irrelevant mAb, combination of these mAbs could significantly inhibit the association of 125I-HDL (32 to 43%) as could polyclonal antibodies (up to 95%). These results are compatible with the concept of HDL binding to these cells via the nonexclusive interaction of each of the amphipathic alpha-helical repeats of apoA-I. When the same approach was applied to block the association of 3H-**cholesteryl** ether (CE)-labeled HDL to HepG2 cells, each anti-apoA-I could inhibit by 15 to 25% the cellular association of **cholesteryl** ether while mAbs in combination or polyclonal antibodies could inhibit this association up to 45% or 60%, respectively. The **cholesteryl** ether radioactivity that remained associated with the cells (40%) in the presence of polyclonal antibodies could be effectively blocked by addition of an antibody against the receptor binding domain of apoE (1D7). Therefore, the differential cellular association of **cholesteryl** ether compared to apolipoprotein can be explained by the presence of apoE secreted by HepG2 and apoE or apoB/E receptors. Thus, we conclude that the optimum uptake of both **cholesteryl** ether and apoA-I of HDL by cells requires the accessibility of the entire apoA-I and the cooperative binding of the

amphipathic alpha-helical repeats to HepG2 cell membranes. This type of interaction would explain the competitive binding observed for apoA-I, -A-II, and -A-IV by others.

L25 ANSWER 36 OF 45 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 92276975 MEDLINE
DOCUMENT NUMBER: 92276975 PubMed ID: 1667793
TITLE: Apolipoprotein A-I decreases neutrophil degranulation and superoxide production.
AUTHOR: Blackburn W D Jr; Dohlman J G; Venkatachalapathi Y V; Pillion D J; Koopman W J; Segrest J P; Anantharamaiah G M
CORPORATE SOURCE: Department of Medicine, University of Alabama, Birmingham 35294.
CONTRACT NUMBER: HL-34343 (NHLBI)
SOURCE: JOURNAL OF LIPID RESEARCH, (1991 Dec) 32 (12) 1911-8. Journal code: 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920710
Last Updated on STN: 19920710
Entered Medline: 19920701

AB Neutrophils participate in the acute phase response and are often associated with tissue injury in a number of inflammatory disorders. The acute phase response is accompanied by alterations in the metabolism of apolipoprotein A-I and high density lipoprotein (HDL). Structural considerations led to studies investigating the effect of purified HDL and apolipoprotein A-I on neutrophil degranulation and superoxide production. Apolipoprotein A-I but not HDL inhibited **IgG**-induced neutrophil activation by about 60% as measured by degranulation and superoxide production. This suggests that the lipid-associating **amphipathic helical** domains of **apolipoprotein A-I** mediate this effect. In support of this was finding inhibitory effects with two synthetic model lipid-associating amphipathic helix peptide analogs. **Apolipoprotein A-I**, containing tandem repeating **amphipathic helical** domains, was approximately ten times more effective than the two peptide analogs and inhibited neutrophil activation at well below physiologic concentrations. Competitive binding studies indicate that resting neutrophils have approximately 190,000 (Kd = 1.7 x 10(-7)) binding sites per cell for apolipoprotein A-I, consistent with a ligand-receptor interaction. These observations suggest that apolipoprotein A-I may play an important role in regulating neutrophil function during the inflammatory response.

L25 ANSWER 37 OF 45 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 91277026 MEDLINE
DOCUMENT NUMBER: 91277026 PubMed ID: 1647394
TITLE: Inhibition of virus-induced cell **fusion** by **apolipoprotein A-I** and its **amphipathic** peptide analogs.
AUTHOR: Srinivas R V; Venkatachalapathi Y V; Rui Z; Owens R J; Gupta K B; Srinivas S K; Anantharamaiah G M; Segrest J P; Compans R W
CORPORATE SOURCE: Department of Microbiology, University of Alabama, Birmingham 35294.
CONTRACT NUMBER: AI 23611 (NIAID)
AI 25784 (NIAID)

CA 40440 (NCI)
+
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (1991 Feb) 45 (2) 224-37.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910818
Last Updated on STN: 19910818
Entered Medline: 19910726

AB Apolipoprotein A-I (apoA-I), the major protein component of serum high-density lipoproteins (HDL), was found to inhibit herpes simplex virus (HSV)-induced cell fusion at physiological (approximately 1 microM) concentrations, whereas HDL did not exert any inhibitory effect. Lipid-associating, synthetic amphipathic peptides corresponding to residues 1-33 (apoA-I[1-33]) or residues 66-120 (apoA-I[66-120]) of apoA-I, also inhibited HSV-induced cell fusion, whereas a peptide corresponding to residues 8-33 of apoA-I (apoA-I[8-33]), which fails to associate with lipids, did not exert any inhibitory effect. These results suggest that lipid binding may be a prerequisite for peptide-mediated fusion inhibition. Consistent with this idea, a series of lipid-binding 22-amino-acid-residue-long synthetic amphipathic peptides that correspond to the amphipathic helical domains of apoA-I (A-I consensus series), or 18-residue-long model amphipathic peptides (18A series), were found to exert variable levels of fusion-inhibitory activity. The extent of fusion-inhibitory activity did not correlate with hydrophobic moment, hydrophobicity of the nonpolar face, helix-forming ability, or lipid affinity of the different peptides. Peptides in which the nonpolar face was not interrupted by a charged residue displayed greater fusion-inhibitory activity. Also, the presence of positively charged residues at the polar-nonpolar interface was found to correlate with higher fusion-inhibitory activity.

L25 ANSWER 38 OF 45 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 91009819 MEDLINE
DOCUMENT NUMBER: 91009819 PubMed ID: 2170446
TITLE: **Apolipoprotein A-I** and its **amphipathic helix** peptide analogues inhibit human immunodeficiency virus-induced syncytium formation.
AUTHOR: Owens B J; Anantharamaiah G M; Kahlon J B; Srinivas R V; Compans R W; Segrest J P
CORPORATE SOURCE: Department of Microbiology, University of Alabama, Birmingham 35294.
CONTRACT NUMBER: AI-25784 (NIAID)
CA-40440 (NCI)
HL-34343 (NHLBI)
+
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1990 Oct) 86 (4) 1142-50.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 19910117

Search completed by David Schreiber 308-4292

Last Updated on STN: 19970203
Entered Medline: 19901121

AB The envelope (membrane) glycoprotein of HIV is essential for virus attachment and entry into host cells. Additionally, when expressed on the plasma membrane of infected cells, the envelope protein is responsible for mediating cell-cell fusion which leads to the formation of multinucleated giant cells, one of the major cytopathic effects of HIV infections. The envelope glycoproteins of HIV contain regions that can fold into amphipathic alpha-helixes, and these regions have been suggested to play a role in subunit associations and in virus-induced cell fusion and cytopathic effects of HIV. We therefore tested the possibility that amphipathic helix-containing peptides and proteins may interfere with the HIV amphipathic peptides and inhibit those steps of HIV infection involving membrane fusion. Apolipoprotein A-I, the major protein component of high density lipoprotein, and its amphipathic peptide analogue were found to inhibit cell fusion, both in HIV-1-infected T cells and in recombinant vaccinia-**virus-infected** CD4+ HeLa cells expressing HIV envelope protein on their surfaces. The amphipathic peptides inhibited the infectivity of HIV-1. The inhibitory effects were manifest when the virus, but not cells, was pretreated with the peptides. Also, a reduction in HIV-induced cell killing was observed when **virus-infected** cell cultures were maintained in presence of amphipathic peptides. These results have potential implications for HIV biology and therapy.

L25 ANSWER 39 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:231585 HCAPLUS
DOCUMENT NUMBER: 112:231585
TITLE: Mode of assembly of amphipathic helical segments in model high-density lipoproteins
AUTHOR(S): Brasseur, R.; De Meutter, J.; Vanloo, B.; Goormaghtigh, E.; Ruysschaert, J. M.; Rosseneu, M.
CORPORATE SOURCE: Lab. Chim. Phys. Macromol. Interfaces, Univ. Lib. Bruxelles, Brussels, 1050, Belg.
SOURCE: Biochimica et Biophysica Acta (1990), 1043(3), 245-52
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The structure of discoidal apolipoprotein A-I (apoA-I) phospholipid complexes, representing the metabolic precursors of mature high-d. lipoprotein (HDL) particles, was studied by a combination of both a theor. and an exptl. approach. The secondary structure of the complex was detd. by CD measurements, whereas the relative orientation of the apoA-I helical segments and of the phospholipid acyl chains was detd. by polarized attenuated fatal reflection IR measurements. Fluorescence energy transfer between the tryptophan residues of apoA-I and fluorescent phospholipid probes yielded an estn. of the relative topog. of the lipid and apolipoprotein components in discoidal and spherical particles. The theor. approach consisted of the identification of the helical segments in various apoA-I species. These segments were then oriented at a lipid/water interface by minimization of their hydrophobic and hydrophilic transfer energies. The calcn. of the hydrophobicity profiles along the axis of the helixes led to the identification of specific interactions between pairs of helixes. The helixes were further assembled together with the phospholipids by specific interactions between pairs of helixes. The helixes were further assembled together with the phospholipids by computer modeling, enabling an estn. of the dimensions of the complex. The combination of the exptl. and theor. results yielded a model for discoidal apolipoprotein-phospholipid complexes, in which the amphipathic

helical segments were oriented along the edges of the disks. Such a model could be extended to the conversion of these complexes into mature spherical HDL, though the formation of a **cholesteryl** ester core.

L25 ANSWER 40 OF 45 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 90232750 MEDLINE
DOCUMENT NUMBER: 90232750 PubMed ID: 2158697
TITLE: Antiviral effects of **apolipoprotein A-I** and its synthetic **amphipathic** peptide analogs.
AUTHOR: Srinivas R V; Birkedal B; Owens R J; Anantharamaiah G M; Segrest J P; Compans R W
CORPORATE SOURCE: Department of Microbiology, University of Alabama, Birmingham 35294.
CONTRACT NUMBER: AI 23611 (NIAID)
AI 25784 (NIAID)
CA 40440 (NCI)
+
SOURCE: VIROLOGY, (1990 May) 176 (1) 48-57.
Journal code: 0110674. ISSN: 0042-6822.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900706
Last Updated on STN: 19900706
Entered Medline: 19900525

AB Apolipoprotein A-I (apo A-I), the major protein component of serum high density lipoproteins, was found to inhibit herpes simplex virus (HSV)-induced cell fusion at physiological (approximately 1 microM) concentrations. An 18 amino acid-long synthetic **amphipathic** alpha-**helical** peptide analog of **apo A-I** (18A) was also found to inhibit HSV-induced cell fusion at similar concentration (approximately 2 microM). Dimers of 18A connected via a proline (37pA) or an alanine (37aA) residue also inhibited virus-induced cell fusion at similar concentration, suggesting that the presence of a proline turn does not influence the antiviral activity of the amphipathic peptides. However, a peptide analog 18R, in which the distribution of charged residues was reversed, inhibited virus-induced cell fusion only at a higher (approximately 125 microM) concentration, suggesting that the anti-viral activity of the amphipathic peptide is strongly influenced by the nature of the charge distribution at the polar-nonpolar interface. Consistent with their ability to inhibit virus-induced cell fusion, the peptides inhibited the spread of HSV infection as demonstrated by a 10-fold reduction in the **virus** yield, when **virus-infected** cells were maintained in the presence of amphipathic peptides. The amphipathic peptides also inhibited penetration of virus into cells, but did not exert any effect on virus adsorption. A nearly complete inhibition of virus penetration was observed when the virus, or both virus and cells, was pretreated with the peptide, suggesting that the peptides may have a direct effect on the virus. The results indicate that amphipathic helices may be useful in designing novel antiviral agents that inhibit penetration and spread of enveloped viruses.

L25 ANSWER 41 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1988:452484 BIOSIS
DOCUMENT NUMBER: BR35:93364

Search completed by David Schreiber 308-4292

Kam 09/840,669

TITLE: COOPERATIVITY IN MULTIPLE **AMPHIPATHIC** HELICAL DOMAINS OF **APOLIPOPROTEIN A-I**

AUTHOR(S): SEGREST J P; GAWISH A; IQBAL M; BROUILLETTE C G; GUPTA K B; ANANTHARAMAIAH G M

CORPORATE SOURCE: DEP. MED., UNIV. ALA. AT BIRMINGHAM MED. CENT., BIRMINGHAM, ALA. 35294, USA.

SOURCE: MARSHALL, G. R. (ED.). PEPTIDES: CHEMISTRY AND BIOLOGY; TENTH AMERICAN PEPTIDE SYMPOSIUM, ST. LOUIS, MISSOURI, USA, MAY 23-28, 1987. XXXIII+690P. ESCOM SCIENCE PUBLISHERS B.V.: LEIDEN, NETHERLANDS. ILLUS, (1988) 0 (0), 369-371. ISBN: 90-72199-01-4.

FILE SEGMENT: BR; OLD

LANGUAGE: English

L25 ANSWER 42 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:227210 HCAPLUS

DOCUMENT NUMBER: 110:227210

TITLE: Cooperativity in multiple **amphipathic** helical domains of **apolipoprotein A -I**

AUTHOR(S): Segrest, Jere P.; Gawish, Ali; Iqbal, M.; Brouillette, Christie G.; Gupta, Kiran B.; Anantharamaiah, G. M.

CORPORATE SOURCE: Med. Cent., Univ. Alabama, Birmingham, AL, 35294, USA

SOURCE: Pept.: Chem. Biol., Proc. Am. Pept. Symp. 10th (1988) , Meeting Date 1987, 369-71. Editor(s): Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth. CODEN: 56MDA6

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review with 6 refs. on the repetitive .alpha.-helical domain of apolipoprotein A-1 (apo A-1) and its role in the lipid-assocg. properties of the protein and its ability to act as a cofactor of the enzyme lecithin-**cholesterol** acyltransferase. Expts. are described which use a 22-mer consensus amphipathic helix and single-amino-acid variants of it to explore the properties of this domain with respect to these 2 functions of apo A-1.

L25 ANSWER 43 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1988:192813 BIOSIS

DOCUMENT NUMBER: BR34:96000

TITLE: STUDIES OF SYNTHETIC ANALOGUES OF THE **AMPHIPATHIC** HELIX ANALOGUES OF **APOLIPOPROTEIN A-I** CONSENSUS DOMAIN.

AUTHOR(S): ANANTHARAMAIAH G M; GAWISH A; IQBAL M; GUPTA K B; BROUILLETTE C G; CHEN C-H; SEGREST J P

CORPORATE SOURCE: UNIV. ALABAMA MED. CENT., BIRMINGHAM, ALA.

SOURCE: 41ST ANNUAL MEETING OF THE AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS (COUNCIL ON ARTERIOSCLEROSIS), ANAHEIM, CALIFORNIA, USA, NOVEMBER 1987. ARTERIOSCLEROSIS, (1987) 7 (5), 508A. CODEN: ARTRDW. ISSN: 0276-5047.

DOCUMENT TYPE: Conference

FILE SEGMENT: BR; OLD

LANGUAGE: English

L25 ANSWER 44 OF 45 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 20

ACCESSION NUMBER: 1985:333376 BIOSIS

Search completed by David Schreiber 308-4292

Kam 09/840,669

DOCUMENT NUMBER: BA80:3368
TITLE: COMPARATIVE ANALYSIS OF REPEATED SEQUENCES IN RAT APOLIPOPROTEINS A-I A-IV AND E.
AUTHOR(S): BOGUSKI M S; ELSHOURBAGY N; TAYLOR J M; GORDON J I
CORPORATE SOURCE: DEP. BIOL. CHEM., WASHINGTON UNIV. SCH. MED., ST. LOUIS, MO 63110.
SOURCE: PROC NATL ACAD SCI U S A, (1985) 82 (4), 992-996. CODEN: PNASA6. ISSN: 0027-8424.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB To understand the structural, functional and evolutionary relationships among the principal protein components of rat high density lipoprotein particles, a systematic comparative analysis was made of the primary structures of apolipoproteins (apo)-A-I, -A-IV and -E. Human apo-A-I and rat apo-A-IV were shown previously to contain repeated sequences that presumably arose by intragenic duplication of 11- or 22-amino acid **amphipathic** segments. For **apo-A-I**, these segments are thought to be the structures responsible for lipid binding and activation of lectithin:**cholesterol** acyltransferase. From an analysis of the sequence of a full-length c[complementary]DNA clone, rat apo-A-I is shown to contain 8 tandem repetitions of a 22-amino acid segment. Compared with human apo-A-I, the rat protein has undergone 3 deletions, 2 of which involve multiple amino acids in the repeated sequence domain. This disruption of the periodic structure of the protein raises the possibility of species-specific variation in the ability of rat apo-A-I to interact with high density lipoproteins and activate lecithin:**cholesterol** acyltransferase. Statistical analysis of the structure and organization of repeated sequences in apo-A-I, -A-IV and -E demonstrates that all 3 proteins are paralogous members of a dispersed gene family. Despite overall similarity in sequence evolved at different rates. Diversification of a duplicated ancestral sequence has resulted in 3 lipid-binding proteins with distinct and shared functions.

L25 ANSWER 45 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1976:588089 HCAPLUS
DOCUMENT NUMBER: 85:188089
TITLE: Molecular packing of high density lipoproteins: a postulated functional role
AUTHOR(S): Segrest, Jere P.
CORPORATE SOURCE: Med. Cent., Univ. Alabama, Birmingham, AL, USA
SOURCE: FEBS Letters (1976), 69(1), 111-15 CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Theor. calcns. of the mol. packing of plasma high-d. lipoproteins (HDL2 and HDL3), using known mol. parameters and assuming a micellar structure of spherical form, showed that the mol. mobility of the terminal 80% of the fatty chains of a phospholipid mol. depends entirely on the packing of the lipid mols., particularly **cholesteryl** ester, in the HDL particle. However, the mobility of the polar head group and the 1st few groups of the fatty acyl chains is substantially affected by protein-lipid assocns. Based on these results, (1) the contribution of electrostatic forces to protein-lipid interactions in HDL varies inversely with the nature of lipid packing, and (2) the reversibility of apolipoprotein **amphipathic** helix-phospholipid assocns. (predominantly involving **apo A-I**) is the means of controlling the packing d. of the polar phospholipid head groups. (Amphipathic helixes are those regions of the polypeptide chain assocg. with and complementary to the polar-nonpolar interface of hydrated bulk phospholipid). The

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packing d. of the polar phospholipid head groups in HDL, in turn, is related to the surface free energy of the particle. The surface free energy apparently controls the rate of exchange of phospholipid and **cholesterol** between lipoproteins and cell membranes.